FIELD TESTING GENETICALLY-ENGINEERED ORGANISMS

HEARING

BEFORE THE

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

OF THE

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY U.S. HOUSE OF REPRESENTATIVES

ONE HUNDREDTH CONGRESS

SECOND SESSION

MAY 5, 1988

[No. 108]

Printed for the use of the
Committee on Science, Space, and Technology.

U.S. GOVERNMENT PRINTING OFFICE

88-743 ⇆ WASHINGTON : 1988

For sale by the Superintendent of Documents, Congressional Sales Office
U.S. Government Printing Office, Washington, DC 20402

H701-4

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

ROBERT A. ROE, New Jersey, *Chairman*

GEORGE E. BROWN, JR., California
JAMES H. SCHEUER, New York
MARILYN LLOYD, Tennessee
DOUG WALGREN, Pennsylvania
DAN GLICKMAN, Kansas
HAROLD L. VOLKMER, Missouri
BILL NELSON, Florida
RALPH M. HALL, Texas
DAVE McCURDY, Oklahoma
NORMAN Y. MINETA, California
BUDDY MacKAY, Florida
TIM VALENTINE, North Carolina
ROBERT G. TORRICELLI, New Jersey
RICK BOUCHER, Virginia
TERRY L. BRUCE, Illinois
RICHARD H. STALLINGS, Idaho
JAMES A. TRAFICANT, JR., Ohio
JIM CHAPMAN, Texas
LEE H. HAMILTON, Indiana
HENRY J. NOWAK, New York
CARL C. PERKINS, Kentucky
C. THOMAS McMILLEN, Maryland
DAVID E. PRICE, North Carolina
DAVID R. NAGLE, Iowa
JIMMY HAYES, Louisiana
DAVID E. SKAGGS, Colorado
PAUL E. KANJORSKI, Pennsylvania
GEORGE J. HOCHBRUECKNER, New York

MANUEL LUJAN, JR., New Mexico*
ROBERT S. WALKER, Pennsylvania
F. JAMES SENSENBRENNER, JR., Wisconsin
CLAUDINE SCHNEIDER, Rhode Island
SHERWOOD L. BOEHLERT, New York
TOM LEWIS, Florida
DON RITTER, Pennsylvania
SID MORRISON, Washington
RON PACKARD, California
ROBERT C. SMITH, New Hampshire
PAUL B. HENRY, Michigan
HARRIS W. FAWELL, Illinois
D. FRENCH SLAUGHTER, JR., Virginia
LAMAR SMITH, Texas
ERNEST L. KONNYU, California
JACK BUECHNER, Missouri
JOEL HEFLEY, Colorado
CONSTANCE A. MORELLA, Maryland
CHRISTOPHER SHAYS, Connecticut

HAROLD P. HANSON, *Executive Director*
ROBERT C. KETCHAM, *General Counsel*
CAROLYN C. GREENFELD, *Chief Clerk*
R. THOMAS WEIMER, *Republican Staff Director*

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

JAMES H. SCHEUER, New York, *Chairman*

TIM VALENTINE, North Carolina
DAVE McCURDY, Oklahoma
HENRY J. NOWAK, New York
C. THOMAS McMILLEN, Maryland
GEORGE E. BROWN, JR., California
GEORGE J. HOCHBRUECKNER, New York

CLAUDINE SCHNEIDER, Rhode Island
ROBERT C. SMITH, New Hampshire
PAUL B. HENRY, Michigan
JOEL HEFLEY, Colorado

*Ranking Republican Member.

CONTENTS

WITNESSES

	Page
May 5, 1988:	
Dr. Luther Val Giddings, Office of Technology Assessment	3
Dr. James Wyngaarden, Biotechnology Science Coordinating Committee and Director, National Institutes of Health; Dr. John A. Moore, Assistant Administrator, Office of Pesticides and Toxic Substances, Environmental Protection Agency; and Dr. Kenneth Gilles, Assistant Secretary for Marketing and Inspection Services, U.S. Department of Agriculture	41

FIELD TESTING GENETICALLY-ENGINEERED ORGANISMS

THURSDAY, MAY 5, 1988

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY,
SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE
RESEARCH AND ENVIRONMENT,
Washington, D.C.

The subcommittee met, pursuant to notice, at 2:17 p.m., in Room 2325, Rayburn House Office Building, the Honorable James H. Scheuer [chairman of the subcommittee] presiding.

Mr. SCHEUER. The Subcommittee on Natural Resources, Agriculture Research and Environment will come to order, and I wish to apologize for the delay. As you just saw, there was a roll call vote which I had to cover.

Today, the subcommittee will review the findings contained in a report just issued by the Office of Technology Assessment entitled "Field Testing Genetically-Engineered Organisms—Genetic and Ecological Issues." The committee feels that OTA did an exemplary job.

We will then also review the efforts of the Federal Government to regulate and review proposals for field testing of genetically-engineered organisms.

Since the publication of the Coordinated Framework for the Regulation of Biotechnology was published two years ago, what has happened since mid-1986?

The OTA report addresses a controversy that has been raging for the last five years when scientists first proposed to bring genetically-engineered organisms from the lab to the field for testing. Some scientists and environmental groups have expressed concern that once released into the environment, these genetically-engineered microbes could multiply and spread, perhaps destroying other organisms and disrupting sensitive ecological systems. They feared what would happen when the gene was released from the bottle. They pointed to the disastrous introduction to non-indengenous organisms such as the starling, the chestnut tree blight, and kudzu.

Other scientists responded that the vast majority of planned introductions of new animals and plant species have been highly beneficial, including most of the crops now commonly grown in the United States.

The central question was: Could the risks of field testing be predicted adequately in advance? The OTA has now completed the most thorough and indpendent analysis to date of the potential

problems associated with small-scale field testing of genetically-altered, genetically-engineered substances.

The main conclusion of the report is that adverse environmental effects are unlikely from any such small-scale field tests of the kind and order of magnitude likely to be proposed in the near future. This finding provides us with reassurance that we can begin to move ahead safely to develop this technology.

Of course, there are serious and important questions remaining unanswered. The application of these findings to large-scale tests or commercial use are limited and, to some extent, unknown. But the small-scale field tests are needed to answer some of these questions.

There also remain serious questions about the adequacy of the federal regulation. Nearly four years ago, the Administration convened an interagency group to ensure adequate federal regulation of biotechnology. In December of 1984, the group published the first proposed Coordinated Framework under which biotechnology products would be regulated under existing statutes.

In June of '86, the so-called final Coordinated Framework was published. As hearings before our subcommittee and subsequent events together demonstrated, however, the Framework was far from final. It wasn't a Final Coordinated Framework at all. Within six months, the Agriculture Department had scrapped this proposal and published a new one. EPA never published rules needed to make its proposal final, and, as I suspect we will hear today, EPA is now contemplating throwing out a large part of its '86 proposal altogether.

The Biotechnology Science Coordinating Committee, the so-called BSCC, which promised two years ago to finish its critical work in defining key terms such as "environmental release," has yet to publish anything. In short, we seem to be still far away from having in place any firm, certain, predictable rules about how biotechnology products are going to be regulated, and this leaves industry in a terrible dilemma. They don't have a road map. Yet products continue to be reviewed and approved for release, and according to information compiled by this subcommitte, since October 1986, the U.S. Department of Agriculture and EPA have approved 34 field tests for genetically-altered microbes and plants. Twenty-five applications are still pending. We seem to be muddling through in spite of the continuing uncertainty about federal guidelines.

But it is doubtful whether this situation will be satisfactory in the future when the number of biotechnology applications are expected to increase dramatically.

So we will be interested in discussing this issue today in more detail with our witnesses from the federal agencies.

The first witness will be the manager of the Office of Technology Assessment Report, a very splendid report, Dr. Luther Val Giddings.

Dr. Giddings, why don't you take eight or ten minutes informally to review the current situation and with the knowledge that your prepared testimony will be printed in full in the record.

So please proceed.

STATEMENT OF DR. LUTHER VAL GIDDINGS, OFFICE OF TECHNOLOGY ASSESSMENT

Dr. GIDDINGS. Thank you. It's my pleasure to be here. Before beginning with any remarks, I need to thank two groups of people, first of all the OTA staff who contributed to this report, and they include Counselor Kevin O'Connor, Dr. Robyn Nishimi, Dr. Gary Ellis, Dr. Robert Friedman, and I also need to point out that in convening this hearing and in releasing the report, working with your staff on the committee, it has been a genuine pleasure to work with them. They are without exception competent, sharp, and a great deal of fun to work with. I think they've done a splendid job, and that applies both to the majority and minority staff. It's been a real pleasure.

Mr. SCHEUER. Thank you very much.

Dr. GIDDINGS. The objectives of the study, as I indicated when we released the report yesterday, were quite simple. First and foremost, we wanted to provide a qualitative answer to the question of what level of risk is posed by planned introductions of genetically-engineered organisms into the environment. And having answered or reached the conclusion in answer to that question, we wanted to provide in our study the scientific information and reasoning by which we arrived at the conclusion, and second, we wanted to provide additional information in a framework that would be useful to the regulatory agencies in developing appropriate mechanisms for review and regulation.

The conclusions of the report we discussed yesterday at some length. I'll briefly reiterate a couple of those right now.

First and foremost, we concluded that while there are reasons for caution, there is no cause for alarm at the prospect of planned introductions of engineered organisms for environmental purposes.

The wide variety of possible applications of such organisms—plants, animals, and microbes—complicates the regulatory picture for federal regulatory agencies enormously and serves to highlight the need for a flexible system of review and of regulation.

As experience accumulates with early field tests, most of which seem to involve very, very low levels of risk in and of themselves, one of the important tasks for regulators will be to avoid letting a situation develop whereby the early experiences, which are likely to be largely positive, it will be important to avoid a situation where regulators are lulled into a false sense of complacency whereby when later on more ambitious applications become possible, they might not receive the appropriate level of review or scrutiny.

We developed a series of potential criteria that could be used in reviewing applications for permission to field test, and we discuss them at some length in the report and the reasons we feel they are valid. The gentlemen that will be appearing before you in the panel to follow me are far more expert on such questions than I, and I will leave the majority of that discussion to them.

I think at this point I could just conclude my remarks and tell you that I'd be happy to entertain any questions that you might have. I know your staff has put together—the last time I saw it, it

looked like a pretty good list, so if you have any questions, I'd be happy to deal with them now.

[The prepared statement of Dr. Luther Val Giddings follows:]

TESTIMONY OF L. VAL GIDDINGS, PH.D.
ANALYST AND STUDY DIRECTOR
OFFICE OF TECHNOLOGY ASSESSMENT, U.S. CONGRESS
BEFORE THE SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE
RESEARCH AND ENVIRONMENT
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
U.S. HOUSE OF REPRESENTATIVES

FIELD TESTING ENGINEERED ORGANISMS: ON MOVING FORWARD

May 5, 1988

Mr. Chairman,

My name is Val Giddings. I am an analyst at the Office of Technology Assessment, where I have directed the project on environmental applications of genetically engineered organisms. This project is part of our ongoing assessment of New Developments in Biotechnology, of which this committee was one of the requestors over two years ago. Yesterday our report on this issue, Field Testing Engineered Organisms: Genetic and Ecological Issues, was released at a press conference sponsored by this committee. Before briefly summarizing the conclusions of our report and discussing what it suggests are some of the next steps that might be taken in this area, I would like publicly to thank the extremely competent OTA staff who contributed to the report: Kevin O'Connor, Robyn Nishimi, Gary Ellis, and Bob Friedman.

The need for congressional oversight to track the intentions and the actions of regulatory agencies with jurisdiction or other responsibilities in this area was a strong and consistent thread running through OTA's discussion of issues and options for congressional action in the study just released. It has been an honor to work with your staff on this and other subcommittees of the full committee, both majority and minority, who have been, without exception, competent, professional, and a delight to work with.

The conclusions of our report received a good deal of attention yesterday. I will briefly reiterate a few of them here before moving to a brief discussion of what the next

steps appear to be, for Congress and the regulatory agencies.

A daunting array of different organisms is being or can be genetically altered by the techniques of modern biotechnology to serve particular environmental purposes. These include vaccines engineered to protect against human and animal diseases; agricultural crops engineered for increased resistance to disease, insect pests, or herbicides; crops engineered for increased growth rates, improved nutritional qualities, taste, or enhanced tolerance to environmental stresses; microbes engineered to reduce crop losses to frost or to improve environmental quality by degrading toxic wastes; and many other environmental applications.

OTA finds that while there are reasons to be cautious there is no cause for alarm at the prospect of field-tests of these genetically engineered organisms. Adequate review is now possible, on what is essentially a case-by-case basis. As experience accumulates, a process now well underway, it will become possible for regulatory agencies to move toward more generic forms of risk assessment. By this I mean that all incoming applications for permission to field test need not, a priori, be considered to require the same high degree of scrutiny, as is now pretty much the case. It should become possible fairly soon to sort incoming applications for permission to field-test into categories for which low, medium, or higher levels of scrutiny are appropriate.

Some potential criteria by which this type of sorting might be carried out are discussed in our report, and today you will also have the opportunity to hear the thoughts of representatives of the regulatory agencies who here today. In this context it is appropriate to note that the wide range of organisms that can be altered in different ways to serve a broad variety of purposes highlights the need for a flexible and adaptable system of regulatory review. Questions pertinent to the safety of an application involving an engineered plant may not be identical to questions pertinent to the safety of a microbe engineered to reduce crop loss to frost damage. Regulatory review needs to be sufficiently flexible and adaptable that applications in need of scrutiny recieve the

appropriate level of examination while those not needing detailed review do not consume limited resources.

As industry moves from field-testing towards commercial-scale environmental applications of genetically engineered organisms some of the relevant risk assessment questions may change. Some of these changes will be due to differences in scale of operations between field-tests and commercial applications, but there may be other issues in addition. It will be important for the review processes of the regulatory agencies to be sufficiently flexible and adaptable to deal with changes of this sort, as well.

The final conclusion of our report that I will mention this afternoon has to do with the role of public opinion. Public opinion with respect to biotechnology was the subject of the previous OTA report in this series (Public Perception in Biotechnology; May, 1987). Of the mass of interesting and detailed information contained in that report one item merits repeated mention here. The point is this: there is a need for more than just an adequate mechanism for assessing risk and weighing costs and benefits in reviewing applications for permission to field test engineered organisms. There is a very real need for a mechanism that is not only effective, but is widely perceived to protect the public interest. The regulatory agencies *must* enjoy public confidence. Though a strong industrial sector is in the public interest, agencies should not appear to coddle industry, even though in clearly serving the public agenda they may sometimes appear to be confrontational with industry. But on the other hand, the regulatory agencies should not allow themselves to be intimidated, or assume the public agenda is set, by alarmists and naysayers. Good science and risk assessment can provide a solid foundation for regulatory decisions which allow judgement calls, when needed, to be made and defended. This industry holds too much potential to allow it to suffer a crisis in public confidence stemming from regulatory actions that appear to be ill considered or arbitrary. Nor is the biotechnology industry so strong that it will be able to withstand

erosion of public confidence.

Moving on, there are a number of issues that will become increasingly important in this area in coming months and years. These issues involve a number of questions that will be important for the regulatory agencies to answer or prepare to deal with.

1. Shortly after the Biotechnology Sciences Coordinating Committee was organized under the Coordinated Framework for Biotechnology it moved to provide some consensus decisions on such matters as definitions for "deliberate release" and "engineered organism." It might be appropriate to inquire now of the current chairman how this or other unfinished business of the BSCC is proceeding.

2. It seems clear that most of the planned introductions of engineered organisms likely to take place in the next several years will be, in and of themselves, quite safe, and free of undue risk. It is not certain, however, that this will continue to be the case as the technology advances to the point where more ambitious applications are pursued. It will be important, though it may be difficult, for the regulatory agencies to exercise the proper mix of caution and efficiency and avoid relaxing or streamlining regulatory procedures so much that an ambitious application that might emerge, one that might deserve close scrutiny, could slip through the system without appropriate review. On the other hand, it is clear that not all applications will need the same high level of review. The proper balance between these two poles may sometimes be difficult to find.

3. It might be appropriate to inquire of the chairman of the BSCC what steps are being taken to ensure that important policy issues in the regulation of this new technology do not fall into jurisdictional or other cracks between the various agencies. Let me give a specific example to illustrate this type of issue.

At the same time that USDA exercises its responsibility by evaluating and

approving testing of genetically engineered herbicide resistant plants, which will likely lead to increased herbicide use, EPA struggles with groundwater contamination by some of these same herbicides. Therefore, we have a situation where one agency, acting within its mandate, may be taking actions that would precipitate changes in agronomic practice so as to exacerbate the problems of a sister agency.

It is not now clear that any body reviewing these matters is looking for potential conflicts of this kind. It is also not clear precisely what action, if any, should be taken, or by whom. This is a policy question that requires attention and discussion. It seems that this is the type of problem that the BSCC might evaluate, and it would be good to hear from the Chairman of that body whether he has the necessary tools for framing or suggesting policy in such situations.

There are other questions that could be raised, but in the interests of time I will close my remarks here. Thank you for the opportunity to testify this morning, Mr. Chairman. I look forward to any questions you may have.

Mr. SCHEUER. Thank you very much, Dr. Giddings.

Can you tell us something about the preparation of the report and the review process that it underwent in the process of preparation?

Dr. GIDDINGS. Well, this has been a fairly challengine job for us. We've been working on it at one level or another for upwards of three years. The reason it's taken us this long is we wanted to be very sure that we did not—that when we did come out with something that we felt was worthy of being published, that it contributed to the discussions and dialogue and moved it forward, focused the discussions on areas that are worthy of analysis and did not—and it took us awhile to decide the best way to pursue it.

We opened up with a—in the very early stages, with a joint—with a workshop sponsored jointly by OTA and the National Science Foundation. This was a fairly unusual kind of thing for us to do, and it was done, I must say, at the initiative of David Kingsbury, who is an Assistant Director at NSF and was at that time head of the Biotechnology Sciences Coordinating Committee (BSCC). We convened this workshop at OTA to examine some of the genetic questions that may be relevant to field testing engineered organisms.

After we completed that, we decided it was time to move on to the real heart of the issue, which dealt with ecological questions, and so we solicited contract support from a large number of people in academia and industry with different expertise in ecological sorts of issues. The reason we had such extensive support from ecologists is that in our program we didn't have any ecologists on the staff. Most of us are molecular biologists or geneticists with a variety of different kinds of lab experience. And so we got—we made use of extensive outside contractor support, and we wound up getting to the point where we had a complete draft, first draft, of the entire report, and we began on the outside review process, which was extensive.

In all, we had three major versions of the report go through extensive review from upwards of 200 individuals outside OTA. They spanned the entire gamut of professional expertise in different areas of biotechnology, ecology, genetics, molecular biology, microbiology, and a variety of different ecological and environmental groups, public interest groups, industry and so on.

We perhaps made our job more difficult than we needed to by asking such a broad range of critical outside reviewers. Every one of the written comments that we received—and there were over 140 on different versions of the draft—we read not once but several times, took the comments very seriously, acted to meet objections raised to ways we had articulated things in the earlier drafts and where we found the comments that we received to have merit. Where we didn't, we tried to articulate the points that we made in such a way not to arouse unnecessary disputes.

The final report is rather more diplomatic than earlier versions, but I think that the substance remains essentially the same.

At the end, when we had effectively completed our work, because of the controversial nature of the topic and some continuing objections to some of the language in the report from different ends of the spectrum of opinion on the issue, the Director, Jack Gibbons,

convened a special ad hoc review group of four individuals from outside the agency that further reviewed our efforts and gave us some additional suggestions as to how to minimize misinterpretation, and we acted on those and wound up publishing the version that you have before you now.

So we went through an extensive process of outside review and tapping outside resources, and we hope it wound up being successful.

Mr. SCHEUER. Well, looking at the list of your New Developments in Biotechnology Advisory Panel, your field testing genetically-engineered organisms OTA project staff, and especially your contractor group and the membership of your OTA/National Science Foundation workshop participants, it does seem to me that you've gone to extraordinary lengths to get the comments from an unusual wide spectrum of experts in the field, and we commend you for that.

Dr. GIDDINGS. Thank you.

Mr. SCHEUER. How does your report differ from the recently issued National Academy of Science report on substantially the same subject? I mean, environmental consequences of genetically-engineered organisms.

Dr. GIDDINGS. That's a little bit of a touchy or difficult question for me to respond to. I'm an authority on the OTA report; I'm much less of an authority on the National Academy's report.

I've discussed the Academy's report with its Director, Arthur Kelman, and a number of the five individuals who worked in preparing it, and I think that if I can relay what I understand from them, their objective was somewhat different than OTA's.

They viewed this issue as being an issue where there has been a fair amount of discussion in the public arena that was not entirely germane to the real issues at hand, and they wanted to, I think, really kind of put some oil on troubled waters and refocus the discussion, provide a voice of reassurance.

They produced a short report. Essentially it's a white paper, unusual for the Academy to produce something like this, but it's a short report fairly focused in its conclusions and limited in its discussion, and it's a report that I think served its purpose quite well.

Our objectives, as you know, are to serve the Congress in dealing with these issues, and we tried to produce something that would be most useful to Congress and the way that you work.

Mr. SCHEUER. Well, we think it will be useful. It was a very thorough, in-depth report.

We've had second bells on this next roll call vote, so I'm going to suspend for about fifteen minutes.

[Recess.]

Mr. SCHEUER. I apologize for this seemingly endless proliferation of roll call votes. We're going to have another roll call vote ten minutes after this one is finished. Well, I can stay here another five minutes after that. So fifteen minutes after those two orange lights go off, we'll have another—I'll have to leave.

So what I'd like to do, Dr. Giddings, is at least release your from servitude, okay?

Dr. GIDDINGS. Thank you.

[Laughter.]

Mr. SCHEUER. No, no. Not now. Oh, no.

[Laughter.]

Mr. SCHEUER. No, you're too quick. Life isn't that easy.

Dr. GIDDINGS. As you wish.

[Laughter.]

Mr. SCHEUER. When I have to leave for the next roll call vote, which is in about fifteen minutes.

Dr. GIDDINGS. I knew it was too easy.

Mr. SCHEUER. Right.

[Laughter.]

Mr. SCHEUER. As I read this report, it concentrates on the potential risk associated with small-scale field tests of genetically-engineered organisms.

How soon do you think there are likely to be a significant number of requests for large-scale, full-scale field tests or for commercial use?

Dr. GIDDINGS. That's quite a difficult question. I think I should point out in answering that, the commercial applications or large-scale field tests will be contingent upon the success or the progress that we find with smaller-scale field tests.

It's not unreasonable to expect that within a few years we will see applications for commercial-scale field tests begin to come in, perhaps even within a year or so. I don't expect that it will be a long time before commercial- scale applications are ready for field test.

Mr. SCHEUER. All right. How relevant are the results of a small-scale field test to our appraisal of full- scale field tests or for commercial use?

Dr. GIDDINGS. Well, they are quite relevant, I think, but of course the process of extrapolation is always problematic. There's a great deal of information contained in our study that should be directly relevant to the questions that are involved in the safety or large-scale as well as small-scale field tests.

However, it is possible that some questions might arise for certain large-scale field tests that we did not examine. Generally those kinds of questions would involve esoterica like density-dependent phenomena, things that take place at large concentrations or organisms that don't necessarily take place at smaller concentrations, some things like that. But those sorts of things have been explored by testimony before this committee at some earlier hearings.

Mr. SCHEUER. Are you telling me that at some point as you go from the small-scale field test to a larger test or to commercial use, you hit a kind of critical mass at which point different phenomena take place that we couldn't possibly have perceived from the small-scale field test?

Dr. GIDDINGS. I would say that it's possible that some additional phenomena might take place that it would be hard to gain a clear understanding of necessarily from small tests. But this is not likely to be the case over the entire range of potential applications. This kind of a threshold may be important only in a few types of applications. It's very difficult right now to predict what those would be or where that might take place.

The people from EPA may have a better idea of that, or USDA may have a better idea of that than we do at this point.

Mr. SCHEUER. At this point, I'm going to yield to our ranking minority member, Congressman Claudine Schneider. But first I would like unanimous consent that we will hold the record open for ten or twelve days and submit additional questions to the witness by mail.

There being no objection, so ordered.

[Information to be furnished follows:]

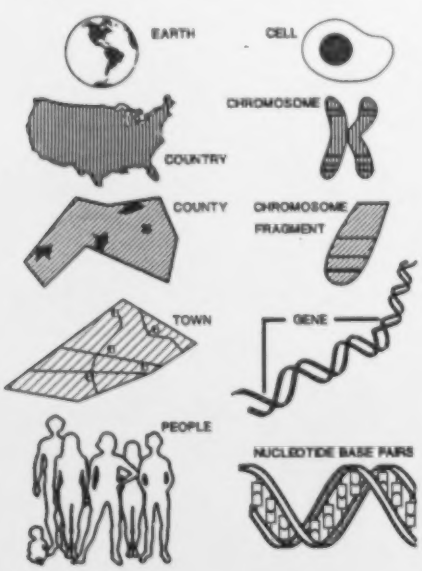
OTA REPORT BRIEF

April 1988

Mapping Our Genes—Genome Projects: How Big? How Fast?

A genome is the total DNA in each cell of an organism. The genome contains the genetic blueprint for the organism's form and function. Genome projects use techniques of molecular genetics to map the structure of all or part of an organism's genome. The goal of genome projects is to collect information systematically about the genetics of entire organisms and to develop new technologies for doing so. Genome projects would lay a foundation for human genetics research in the 21st century. They include several components:

- improvement of genetic databases and linkage among them;
- genetic linkage maps—sets of markers on chromosomes to locate genes of interest for further study;
- ordered sets of stored DNA segments that cover large expanses of chromosomes;
- new technologies to handle, detect, clone, sequence, and purify DNA;
- pilot projects to determine the sequence of DNA in chromosomes or large regions of chromosomes; and
- new computer software and hardware for analysis of genetic map and sequence information.



The principal justifications for genome projects are scientific, although technological spinoff will also result. Genome projects will produce, for example, genetic tests for human diseases, instruments widely useful in biotechnology, and information to develop pharmaceuticals based on knowledge of human genes.

The National Institutes of Health (NIH) and the U.S. Department of Energy (DOE) have special genome programs. NIH's projects, projected at $28 million for 1989, will develop new methods to study the genetics of complex organisms and new tools to analyze resulting data: biological methods, computational methods, and other resources. DOE proposes, in its 1989 budget request for $18 million, to generate sets of DNA representing human chromosomes, to develop methods for computer analysis of genetic data, and to devise instruments for molecular genetics.

NIH funds the largest fraction of genetics research, a large majority of genetics researchers, and most of the relevant research infrastructure. DOE develops instruments, manages large-scale projects, has extensive computer expertise, houses the DNA sequence database, and funds the national laboratories. DOE was the first agency to commit its resources to genome projects explicitly. The National Science Foundation (NSF) is developing several biology centers nationwide, has genetics and instrumentation grant programs comparable in size to DOE's, and has a legislative mandate to coordinate science among Federal agencies.

Are Genome Projects Big Science?

Genome projects would be larger and more directed than most research in biology, but small in scale compared to high-energy physics projects and space programs. Genome projects will require sustained commitments of substantial resources, with more central coordination than is usual in genetics research. A DOE advisory committee and a committee of the National Academy of Sciences have recommended annual budgets of $200 million per year for genome projects. Genome projects would be directly linked to ongoing research in genetics and would produce useful results long before they were completed. New facilities dedicated to genetic mapping and sequencing may or may not prove necessary; technologies yet to be developed will determine the need for such facilities.

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director*.

Each agency thus has a distinct contribution to make to genome projects. Attempts to consolidate authority at a single agency might simplify some management problems, but the difficulty of choosing which agency might delay work, threaten the aggregate budget, and would not solve problems of coordination with foreign and private sector efforts. An alternative option is an interagency working group composed of academic scientists, government agency representatives, industrial scientists, and other experts.

Copies of the OTA report, "Mapping Our Genes—Genome Projects: How Big? How Fast?" are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325 (202) 783-3238. The GPO stock number is 052-003-01106-9; the price is $10.00. Copies of the report for congressional use *are available by calling 4-8996.*

Are Genome Projects Important?

The importance of databases, computer analysis, new technology development, and various types of gene maps is undisputed. These have been called "high-priority normal science," because they address critical research needs and promise to make research more efficient by doing once systematically what would otherwise be done piecemeal. The value of massive sequencing remains in dispute and can be resolved only by pilot projects.

Gene maps and DNA sequence data will be most useful if the entire research community has access to them. This will require special planning by Federal research agencies. Policies of Federal agencies can also affect the rate and magnitude of commercial application. Patent policies of NIH, DOE, and NSF can expedite commercialization of products resulting from federally funded research.

Do Genome Projects Raise Ethical Questions?

Yes, but only indirectly in most cases. The fundamental issues are not new, but emerging genetic technologies will make them salient. Genetic techniques will as a rule permit detection or prediction of disease long before treatments are available, so a gap will arise between diagnosis and therapy. Availability of diagnostic technologies may also intensify the debate about prenatal genetic testing and abortion. Information about human genetics will influence theories about human origins and the relationship of genetic factors to socially desirable (or undesirable) traits. Genetic information has often been used for political purposes in the past; information arising in genome projects could be similarly misused. These are not arguments against research efforts, however. Policies to address such issues can focus on uses, rather than the data and technologies themselves.

International Efforts

Several European governments support genetics research, but none has explicit genome programs except Italy, which has begun a few pilot projects. A privately funded effort will soon begin in the United Kingdom. Japanese government actions have been modest to date, but concern persists that Japan will seize the technological lead from America's advantage in basic genetics. There will likely be international competition to develop new technologies, but new information gained from genome projects will benefit all nations. International cooperation can build on the successes of existing collaborative arrangements among databases and scientific groups.

Principal Organizations Involved in Genome Projects

Organization	Mission	Funding ($000,000s)[a]
National Institutes of Health (Department of Health and Human Services)	Biomedical research	Life sciences: 6,170 Related research: 313 Genome projects: 17.2 NLM biotechnology databases: 3.83
Department of Energy (Office of Health and Environmental Research, Office of Energy Research)	Biological effects of energy production and radiation; use of national laboratory resources	Life sciences: 230 Related research: 7 Genome projects: 12
National Science Foundation (Directorate of Biological, Behavioral, and Social Sciences	Basic scientific research	Life sciences: 206 Related research: 32.7 Genome projects: 0.2
Howard Hughes Medical Institute	Biomedical research	Life sciences: 240 Genetics: 40 Genetic marker maps: 2 to 4 Databases: 2

[a]"Life sciences" figures are estimates for fiscal year 1987; these are total budgets for NIH and HHMI and estimates of relevant programs for NSF and DOE. Figures for "related research" include basic research projects that involve mapping or sequencing, and research infrastructure such as databases and repositories. "Related research" figures are estimates for fiscal year 1987. "Genome projects" figures are estimates for fiscal year 1988, based on appropriations under the December 1987 continuing resolution.

SOURCES: NIH: Rachel Levinson, personal communications, October, November, December 1987, January 1988; DOE: David Smith, personal communications, June, October 1987, January 1988; NSF: David Kingsbury, personal communications, June and November 1987; HHMI: George Cahill, personal communication, January 1988.

OTA REPORT BRIEF

May 1988

Book Preservation Technologies

Even in today's high tech society, books are the principal records of human civilization. Over the centuries, books have become the most reliable and permanent records available, but, in the last century, that reliability has been threatened by the use of "modern" acidic paper, which becomes brittle and unusable in a relatively short time. Books printed since the mid-1800s are deteriorating en masse in libraries the world over.

The U.S. Library of Congress initiated a major preservation program in the early 1970s and developed a mass deacidification process that is now being tested at a pilot plant. Planning is underway to design and construct a full-scale facility that could treat about 1 million books per year.

Photo credit: Library of Congress

Brittle book from the Library of Congress' collection

The Library's process is unique and effective but also presents some new engineering and safety concerns because it makes use of a highly reactive chemical—diethylzinc—as the deacidification agent. OTA's technical review of this program indicates a high potential for success in meeting the Library's stated goals. However, the program is still in the developmental stage with difficult and complex tasks ahead. Despite the credible pilot plant program currently underway, additional work is needed to determine accurate costs for a full-scale plant and how such a plant will be managed. Also, the apparent competition among several firms and institutions for the best deacidification process would make continued evaluation of the relative costs and effectiveness of alternate deacidification processes prudent.

OTA's findings include:

- The diethylzinc (DEZ) mass deacidification process developed by the Library of Congress produces effective and uniform paper deacidification, and leaves an adequate alkaline reserve on treated book papers.
- While substantial life extension benefits of DEZ mass deacidification are generally accepted, more quantitative testing is needed to determine specific benefits to the Library's collection.
- The DEZ deacidification system can be safely operated but some hazards are inherent in that process and risks will always be present. Safety practices will always require careful, consistent top management attention.
- Of those processes for which OTA had sufficient data, no other mass deacidification system meets as many of the Library's criteria for ease and effectiveness as does the DEZ process, but two alternatives merit some consideration (Wei T'o and Bookkeeper). The effectiveness and other aspects of these alternatives must be more carefully checked if they are considered, but present indications are that these alternatives could be lower cost than the DEZ process.

Copies of the OTA report, "Book Preservation Technologies," are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325 (202) 783-3238. The GPO stock number is 052-003-01103-4; the price is $5.00. Copies of the report for congressional use *are available by calling 4-8996.*

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director.*

OTA REPORT BRIEF

May 1988

Field-Testing Engineered Organisms: Genetic and Ecological Issues

To date, genetically engineered organisms have been field-tested about two dozen times in at least 12 States and four foreign countries. Additional field tests will occur in coming months; increasing numbers are expected in the future.

With recombinant DNA techniques, genetic material can be either added to or deleted from organisms to make them serve a wide range of purposes: vaccines to protect against human and animal diseases; agricultural crops with increased resistance to disease, insect pests, or herbicides; crops with increased growth rates, improved nutritional qualities, taste, or enhanced tolerance to environmental stresses; and microbes that reduce crop losses to frost or improve environmental quality by degrading toxic wastes (see table on reverse).

While some of these applications may raise concern and questions of safety for public health or environmental quality, adequate review of planned introductions is currently possible and most problems can be anticipated and prevented. The small-scale field tests proposed or probable within the next several years are not likely to result in an environmental problem that would be widespread or difficult to control. Indeed, realistic small-scale field tests may be the only way to evaluate potential risks from commercial-scale uses of genetically engineered organisms. Results from these field tests will help improve general capabilities for risk assessment and prediction. If small-scale field tests do not identify areas of significant concern, there would be no scientific reason not to proceed with larger-scale field tests or applications.

Planned introductions of genetically engineered organisms into the environment are not, however, without potential risks. Virtually any organism deliberately introduced into a new environment will have a small but real chance of surviving and multiplying. In some cases, an undesirable consequence might follow. Because even simple ecosystems are very complex, the precise prediction of such events and of their consequences is difficult.

With further experience, agencies regulating the release of engineered organisms (principally the Environmental Protection Agency and U.S. Department of Agriculture) should be able to move from the present case-by-case examination of each proposed field test, to a more streamlined system in which specific proposals are assigned to the appropriate level of review (e.g., low, medium, and high).

OTA identified options for congressional action in three major areas of public policy related to this promising new application of biotechnology:

- criteria for review of planned introductions for potential risk,
- administrative mechanisms for applying such review criteria, and
- the research base supporting planned introductions.

•

This special report is the third in a series of reports on New Developments in Biotechnology. Copies of the OTA special report, "Field-Testing Engineered Organisms: Genetic and Ecological Issues," are available from the U.S. Government Printing Office, Washington DC 20402-9325, tel: (202) 783-3238. The GPO stock number is 052-003-01104-2; the price is $7.50. Copies of the report for congressional *use are available by calling 4-8996.*

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director*.

Some Representative Pending and Potential Environmental Applications of Genetically Engineered Organisms

MICRO-ORGANISMS

Bacteria as pesticides. "Ice-minus" bacteria to reduce frost damage to agricultural crops.

Bacteria carrying *Bacillus thuringiensis* toxin to reduce loss of corn crops to black cutworm.

Plant symbionts. Nitrogen-fixing bacteria to increase nitrogen available to plants, and decrease need for fertilizers.

Mycorrhizal fungi to increase plant growth rates by improving efficiency of root uptake of nutrients.

Toxic waste disposal. Bacteria engineered to enhance their existing abilities to degrade compounds found in sludge in waste treatment plants.

Bacteria engineered to enhance their abilities to degrade compounds in landfills, dumps, runoff deposits, and contaminated soils.

Heavy metal recovery. Engineered enhancements possible to several species of bacteria now used to recover metals from low-grade ores (e.g., copper and cobalt).

Pollution control. Possible increased utility of bacteria in purifying water supplies of phosphorus, ammonia, and other compounds.

Viruses as pesticides. Insect viruses with narrowed host specificity or increased virulence against specific agricultural insect pests, including cabbage looper, pine beauty moth, cutworms, and other pests.

Myxoma virus modified so as to restore its virulence against rabbits (which became resistant during early biocontrol efforts in Australia).

Viruses as vaccines.

Vaccines against human diseases including:
- —hepatitis A and B
- —polio
- —herpes simplex (oral and genital)
- —malaria
- —acquired immunodeficiency syndrome
- —rabies
- —respiratory syncitial virus

Vaccines against animal diseases including:
- —swine pseudorabies
- —swine rotavirus
- —vesicular stomatitis (cattle)
- —foot and mouth disease (cattle)
- —bovine rotavirus
- —rabies (cattle, other mammals)
- —sheep foot rot
- —infectious bronchitis virus (chickens)
- —avian erythroblastosis
- —sindbis virus (sheep, cattle, chickens)

Multivalent vaccines. Vaccines possible for antigenically complex diseases such as:
- —malaria
- —sleeping sickness
- —schistosomiasis

PLANTS

Herbicide resistance or tolerance to:

Glyphosate
Atrazine
Sulfonylurea (chlorosulfuron and sulfometuron)
Imidazolinone
Bromoxynil
Phosphinotricin

Disease resistance to:

Crown gall disease (tobacco)
Tobacco mosaic virus (and related viruses)
Potato leaf roll virus

Pest resistance

BT-toxin-protected crops, including tobacco (principally as research tool) and tomato.

Seeds with enhanced anti-feedant content to reduce losses to insects while in storage.

Enhanced tolerance to environmental factors, including:

Salt
Drought
Temperature
Heavy metals

Nitrogen-fixation enhancements

Nonlegumes enhanced to fix nitrogen, independent of association with symbiotic bacteria.

Engineered marine algae

Algae enhanced to increase production of such compounds as B-carotene and agar, or to enhance ability to sequester heavy metals (e.g., gold and cobalt) from seawater.

Forestry

Trees engineered to be resistant to disease or herbicides, to grow faster, or to be more tolerant to environmental stresses.

ANIMALS

Livestock and poultry

Livestock species engineered to enhance weight gain or growth rates, reproductive performance, disease resistance, or coat characteristics.

Livestock animals engineered to function as producers for pharmaceutical drugs, especially of mammalian compounds that require post-synthesis modifications in the cell.

Fish

Triploid salmon produced by heat shock for use as game fish in lakes and streams.

Fish with enhanced growth rates, cold tolerance, or disease resistance for use in aquaculture.

Triploid grass carp for use as aquatic weed control agents.

SOURCE: Office of Technology Assessment, 1986.

OTA REPORT BRIEF

May 1988

Criminal Justice, New Technologies, and the Constitution

New technologies can improve the criminal justice process and make law enforcement more efficient and effective. Some may also infringe on the rights of people accused of or convicted of crime—specific rights guaranteed by the Fourth, Fifth, Sixth, Eighth, and Fourteenth Amendments to the U.S. Constitution—and the rights of all Americans.

Electronic technologies and technologies based on the biological and social sciences are rapidly entering police work—enhancing capabilities, but also increasing opportunities for deliberate or inadvertent misuse. Electronic surveillance technologies challenge the effectiveness of Fourth Amendment protection against unreasonable searches and seizures because information is no longer necessarily embedded in "persons, houses, papers, and effects" as in 1789, and because new technology modifies what the Supreme Court has called "the reasonable expectation of privacy." Biological technologies—such as identification by means of bodily conformations, fluids and tissues, or mental processes—raise similar questions. Computer databases and computer matching have enormously expanded the capability of government to gather and use information about individuals.

The use of conventional weapons by law officials may be challenged as an unnecessary use of deadly force if less-than-lethal weapons, not yet satisfactory for most law enforcement purposes, become highly reliable. What is judicially permissible can change when technology changes.

Criminal justice officials are increasingly using social science research, predictive models, simulation, expert systems, and other computer-assisted techniques to make decisions about arrests, pretrial release, sentencing, probation, and parole. More consistent decisionmaking can support the constitutional values of due process and equal protection of the laws. But scientific techniques derived from the behavior of groups and populations, may, when applied to individuals, be unconstitutionally discriminatory unless used with great discretion.

Pressures to alleviate prison overcrowding encourage the search for alternatives to prison. Today these include privately-run prisons, home arrest monitored by electronic bracelets, and treatment of some offenders with drug and hormone therapy or behavior modification. Some of these may be challenged as cruel and unusual punishments or as violating rights to privacy or due process. But others are clearly preferable to prison, especially since AIDS has been added to the risks already found in prisons. To the extent that these alternatives are dependent on having a job, fixed abode, or steady income, as some now are, they may be challengable on the grounds of equal protection of law.

As records-keeping and -sharing become even more essential to the administration of justice, issues related to data quality and confidentiality become more important. Neither law nor constitutional precedents in this area have yet accommodated to the problems of the information age.

Technological innovations promise significant benefits in reduction of crime and more equitable administration of justice. But some may widen the net of social control and chill the exercise of constitutional rights. Justice Brandeis once said, "Experience should teach us to be most on our guard to protect liberty when the Government's purposes are beneficent." The benefits of these technologies should not be lost through fear of potential abuses; those abuses can be avoided through the diligent attention of citizens, lawmakers, courts, and criminal justice administrators.

Copies of the OTA report, "Criminal Justice, New Technologies, and the Constitution," are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325 (202) 783-3238. The GPO stock number is 052-003-01105-1; the price is $2.75. Copies of the report for **congressional use** *are available by calling 4-8996. Summaries of reports are available at no charge from the Office of Technology Assessment.*

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director.*

OTA REPORT BRIEF

May 1988

Technology and the American Economic Transition: Choices for the Future

The American economy has entered a period of fundamental change. During the next two decades, new technologies, rapid increases in foreign trade, and the changing tastes and values of Americans are likely to reshape virtually every product, every service, and every job in the United States. These forces will shake the foundations of the most secure American businesses.

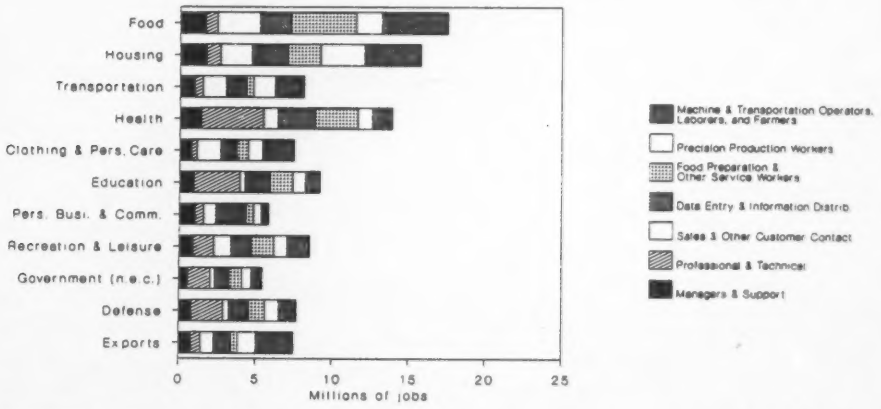
Eight congressional committees asked the Office of Technology Assessment to take a broad look at the opportunities and risks created by the new environment. OTA's response describes the economy as a set of complex networks that convert the skills and savings of Americans into amenities like health, food, education, and recreation (see figure). It also develops a set of specific hypotheses about the way economic networks *could* operate in the future. The analysis makes no attempt to forecast the future. Instead, it attempts to provide the clearest possible description of the available choices and their implications. It measures progress both in terms of income growth, the quality of amenities, and the number and quality of jobs.

The networks emerging in the economy are likely to be relatively decentralized and able to deliver products and services tailored to comparatively small, fast moving markets. Imported products will be used throughout the economy. The economic networks are also likely to be less dependent on natural resources and much more dependent on the intellectual and interpersonal skills of people. They are likely to depend critically on the ability of the Nation's educational system to produce people with versatile skills, and to maintain and upgrade these skills.

The study identifies many of the changes that have already occurred because of this ongoing economic transition. The number of lawyers, scientists, and data-entry clerks needed to supply Americans with food, for example, is now roughly equal to the number of farmers. The mix of purchased goods and services, as well as unpaid personal time, used by Americans to achieve recreation, health and other amenities has also changed. Most of the new jobs created in the last several years have been in managerial, professional, sales, and technical occupations.

In addition, there has been considerable growth in the purchase of services by American businesses and households. Services once provided at home by household members, such as care of children and the elderly, are now purchased. Decline of free time, especially by women as they continue to enter the work force, has

Jobs Required To Provide Amenity in 1984



ABBREVIATIONS: Clothing & Pers. Care = Clothing & Personal Care, Pers. Busi. & Comm. = Personal Business & Communication, n.e.c. = not elsewhere classified.

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director*.

also meant, for example, that more meals are eaten outside the home. At the same time, some services once purchased, such as movies, can now be provided at home (through VCRs). These and other shifts in consumption, production, and employment patterns will continue and perhaps accelerate as changing technology, trade and tastes further influence the shape of the future economic networks.

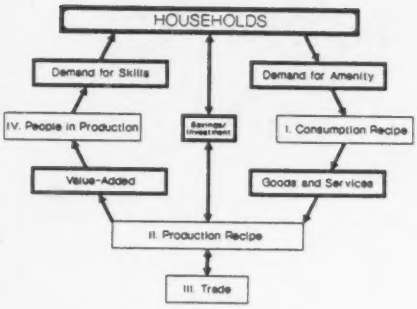
The changes before us offer unprecedented opportunities for growth, but they also contain the seeds of potential stagnation and decline. It is not clear, for example, whether the majority of Americans will be able to find attractive opportunities for work, or whether only a credentialed elite will enjoy such opportunities. Failure to take advantage of emerging technologies and to grasp the new rules of international trade could leave America bypassed by nations that have discovered better ways to profit from innovation.

While fundamental change is underway, few features of the change are inevitable. The Nation's future has probably never been less constrained by the cost of energy or materials or the limits of human strength, dexterity, or memory. Much less depends on physical limits to what *can* be done and much more on what Americans *choose* to do.

One of the most critical issues is whether the flexibility and dynamism essential to progress in the emerging economy will come at the expense of individuals, or whether individuals themselves will become more flexible because of continuous opportunity for learning and growth. In the past it seemed necessary to make a Faustian compact with technology: efficiency could be improved only by sacrificing individuality. Efficiency demanded mass production of uniform products, and a reasonable income often required acceptance of a constraining and narrowly defined occupation. Emerging technology may make it possible to avoid making such choices.

Can America operate a dynamic and growing economy and navigate a transition to a new, more flexible, economic structure without falling into any potential traps? Specifically, can the nation develop a set of marketplace rules that bring private and public goals into greater harmony without stifling the innovation and entrepreneurship needed to reach these goals? Can both workers and investors be given sufficient incentives to undertake major changes in production systems? Can a major transformation be managed so that unavoidable trauma will not uniformly be borne by a single group?

Structure of the Analysis



The assessment argues that the answer to all these questions is yes—but only given an unflinching reexamination of some of the most cherished notions about the way businesses are managed internally, the way networks of enterprises work together, and the way government sets the rules under which businesses and individuals make their choices.

One feature of the transformation seems particularly clear. Returning to an economy like that of the 1960s is not one of our practical choices.

Copies of the OTA report, "Technology and the American Economic Transition: Choices for the Future," are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325 (202) 783-3238. The GPO stock number is 052-003-01096-8; the price is $20.00. Copies of the report for **congressional use** *are available by calling 4-8996. Summaries of reports are available at no charge from the Office of Technology Assessment.*

OTA REPORT BRIEF

May 1988

Infertility: Medical and Social Choices

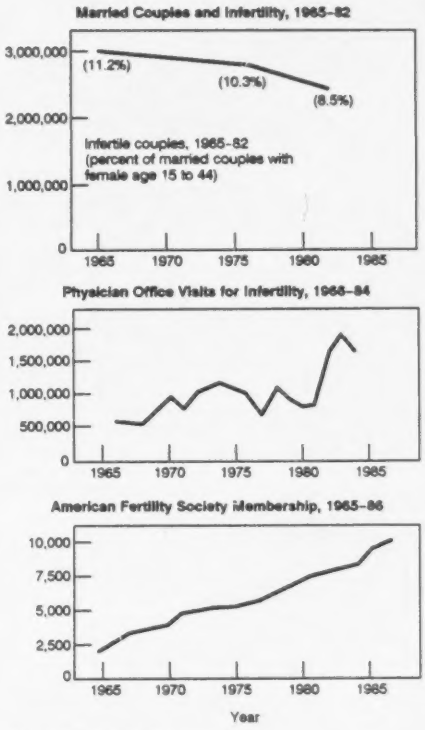
Americans spent an estimated $1 billion on medical care in 1987 to combat infertility (defined as a couple's inability to conceive after 12 months of intercourse without contraception). As many as half the infertile couples seeking treatment are ultimately unsuccessful, despite trying various avenues of treatment.

Among those seeking treatment, 85 to 90 percent are treated with conventional medical or surgical therapies, which are still the most successful and widely used approaches to overcoming infertility. This category includes ovulation induction, surgery, and artificial insemination. Two new, noncoital reproductive technologies—in vitro fertilization (IVF) and gamete intrafallopian transfer (GIFT)—offer hope to infertile couples who could not be successfully treated otherwise. These two techniques are being practiced with increasing frequency, but proficiency varies widely.

Infertility affects an estimated 2.4 million married couples (data from 1982). Although there has been no increase in either the number of infertile couples or the overall incidence of infertility in the population, the number of office visits to physicians for infertility services rose from about 600,000 in 1968 to about 1.6 million in 1984. Concomitant increases occurred in the memberships of the American Fertility Society and other professional organizations for physicians who treat infertile patients.

Preventing infertility is difficult. Nevertheless, an estimated 20 percent of infertility in the United States —that resulting from chlamydia, gonorrhea, or other sexually transmitted diseases—is preventable.

Surrogate motherhood is more a social solution to infertility than a medical technology. An estimated 100



SOURCE: Office of Technology Assessment, 1988

Some Causes of Increasing Requests for Infertility Services in the 1980s

More couples with primary infertility	Increasing proportion of infertile couples seeking care	Increasing number of physicians providing infertility services	More conducive social milieu	Evolution of new reproductive technologies
• Aging of the baby-boom generation • Delayed childbearing; more people in higher risk age groups • Childbearing condensed into shorter intervals • Delayed conception due to prior use of oral contraceptives	• Decreased supply of infants available for adoption • Heightened expectations • Larger number of people in higher income brackets with infertility problems • Larger percent of infertile couples are primarily infertile	• Greater demand from private patients • More sophisticated diagnosis and treatment • At least 169 sites in the United States offering in vitro fertilization or gamete intrafallopian transfer	• Baby-boom generation expects to control their own fertility • Profamily movement • Increased discussion of sexual matters due to the AIDS epidemic • Extensive media coverage	• Artificial insemination • Surrogate motherhood • In vitro fertilization (IVF) • Gamete intrafallopian transfer (GIFT) • Cryopreservation

SOURCE: Adapted from S.O. Aral and W. Cates, Jr., "The Increasing Concern With Infertility: Why Now?" *Journal of the American Medical Association* 250:2327-2331, 1983.

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director*.

surrogate mother arrangements may be concluded annually in the coming years. The legal status of these arrangements is today unsettled, although legislation addressing some aspects of surrogacy has been passed in Louisiana, Arkansas, Nevada, and Kansas. State court decisions have consistently found surrogacy contracts to be unenforceable, even though they have split on whether the contracts are legal.

In addition to offering hope to some infertile couples, in vitro fertilization permits researchers to view for the first time human reproduction in progress. Understanding the interactions between egg and sperm has potentially broad application not only for conception, but for contraception as well. Researchers seeking Federal funding to work in this area, however, have faced the stifling effects of a de facto moratorium since 1980 on Federal funding of research involving human in vitro fertilization.

U.S. public policy related to infertility is difficult to establish because of a wide range of sometimes conflicting ethical views. Concerns focus on three principal ethical issues—the right to reproduce, the moral status of an embryo, and research with patients.

At least eight other nations (Australia, Canada, the Federal Republic of Germany, France, Israel, the Netherlands, Sweden, and the United Kingdom) have enacted legislation or issued major Government reports on assisted reproduction. In the United States, nine policy issues related to infertility confront Congress:

- collecting data on reproductive health;
- preventing infertility;
- information to inform and protect consumers;
- providing access to infertility services;
- reproductive health of veterans;
- transfer of human eggs, sperm, and embryos;
- recordkeeping;
- surrogate motherhood; and
- reproductive research.

Copies of the OTA report, "Infertility: Medical and Social Choices," are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325, (202) 783-3238. The GPO stock number is 052-003-01091-7; the price is $16.00. Copies of the report for congressional use are available by calling 4-8996. Summaries of reports are available from the Office of Technology Assessment and from the U.S. Government Printing Office. The stock number is 052-003-01061-5; the price is $2.00.

Infertility's Emotional Toll

You find yourself experiencing feelings that you have never had before. Sometimes you are depressed when you never used to be, or you avoid situations that have anything to do with children. Your thoughts over the last six months include:

Why is this happening to me?
I must have done something wrong to deserve this.
I have to keep an important part of my life secret.
I have nobody I can talk to about this.
Sex on schedule takes all the joy out of making love.
Nobody understands how I feel, even my spouse.
I'm angry all the time.
I feel as if everything in my life is on hold.
I have a lot of trouble sleeping.
I'm always tired lately.
I've lost my self-confidence.
I feel like a failure in everything in my life.
I feel sad and alone.
I'm afraid my spouse will give up on me.
We don't have fun anymore.
We don't fit in with our friends; they all seem to be into children.
My family can't support me like they used to, especially on special occasions when children are the center of attention.
If I could just stop trying so hard, maybe we could have a baby.

OTA REPORT BRIEF

May 1988

Seismic Verification of Nuclear Testing Treaties

Technologies that were originally developed to study earthquakes may now enable the United States to verify a treaty with the Soviet Union to further limit the testing of nuclear weapons.

Underground nuclear explosions release their energy in less than one-millionth of a second, vaporizing rock and creating vibrations that travel through the Earth as seismic waves. By recording and analyzing these waves, seismology plays a central role in verifying arms control agreements that limit the testing of nuclear weapons.

Present treaties limit the U.S. and U.S.S.R. to testing underground and at yields no greater than 150 kilotons. (One kiloton is approximately the explosive power of 1,000 tons of TNT; the bomb dropped on Hiroshima was approximately 13 kilotons (kt).) Although these treaties have had positive environmental and arms control impacts, they have not prevented the development of new bombs and warheads. Consequently, public interest in a complete test ban or a much lower threshold remains strong and each year a number of proposals are brought before the Congress to further limit the testing of nuclear weapons.

Principal Findings

Monitoring

Seismic monitoring networks are now extremely sophisticated and have remarkable capabilities. A high quality network could detect and identify with confidence nuclear explosions well-below 1 kt, if no attempt were made to muffle the seismic signal or spoof the seismic network. The figure on the reverse side, for example, shows the signal of a 1/4 kt explosion recorded from a distance of 3,800 km. However, a country attempting to test clandestinely would presumably use every means to reduce the size of the seismic signal created by the explosion and fool the monitoring network. For example, a potential evasion method would be to muffle a small clandestine nuclear explosion by setting it off in a large underground cavity, and attribute the muffled signals to a large chemical explosion that is simultaneously set off under the guise of legitimate industrial activity.

Seismic monitoring capability is limited by our ability to demonstrate that all credible evasion scenarios could be defeated. Monitoring small explosions is more difficult because there are more methods of evasion and more innocent signals (e.g., earthquakes and large quarry blasts) from which such a test would need to be distinguished. Countering evasion scenarios should be approached through a combination of seismic methods, treaty constraints, and other monitoring methods. Consequently, the capabilities of any given seismic monitoring network will depend on how the task is approached and what supplementary provisions are negotiated within the treaty.

Ultimately, there will always be a limit to the capability of any given monitoring network, and hence there will always be a threshold below which the uncertainty of any monitoring system will increase. Determining the level that cannot be adequately verified is a political judgment of the point at which the risks of a treaty outweigh its benefits.

How Low Can We Go?

Treaties with low-yield testing limits would require seismic stations throughout the Soviet Union, provisions (e.g., notification, onsite inspection) to handle large chemical explosions, and stringent testing restrictions to limit opportunities for evading the monitoring network. If such restrictions could be negotiated, most experts believe that a high-quality, well-run network of internal stations could confidently monitor a threshold of around 5 kt. Expert opinion about the lowest yields that could reliably be monitored ranges from 1 to 10 kt, depending on judgments about what technical provisions can be negotiated, how much the use of high frequencies will improve our capability, and what levels of confidence are necessary to ensure that the Soviet Union would not risk testing above the threshold. Lower thresholds or even a complete ban could still be considered verifiable if, taking both seismic and non-seismic methods into account, the significance of undetected violations (should they occur) would be outweighed by the benefits of such a treaty.

Soviet Compliance

Extensive statistical studies have examined the distribution of estimated yields of explosions at Soviet test sites. The results conclude that Soviet testing is consistent with compliance with the 150 kt limit of the Threshold Test Ban Treaty. The distribution of Soviet tests indicates that about 10 (out of over 200) Soviet explosions since the signing of the Threshold Test Ban Treaty in 1974 could have estimated yields with central values above the 150 kt threshold limit, depending on how the estimate is made. However, all of these

(over)

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director*.

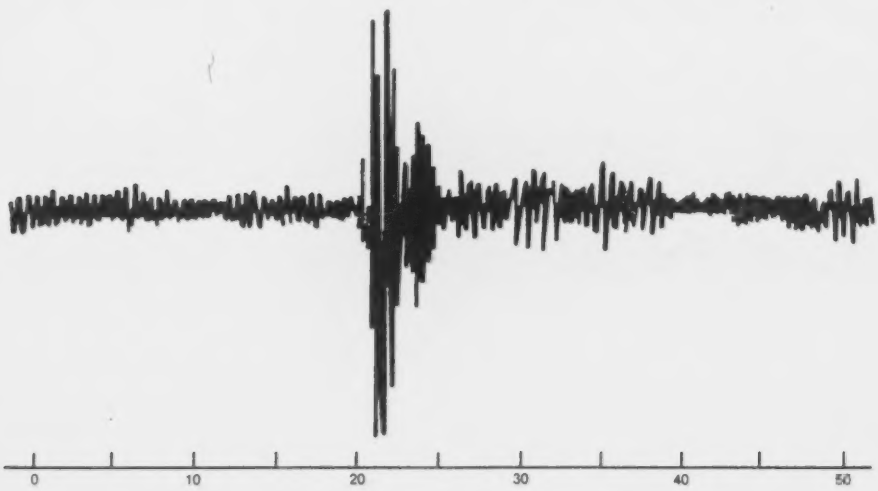
estimates are within the 90 percent confidence level that one would expect if the actual yields were 150 kt or less.

Verification of the TTBT and the PNET

The 1974 Threshold Test Ban Treaty and the 1976 Peaceful Nuclear Explosions Treaty remain unratified in part because of concerns that the size of Soviet explosions cannot be measured with adequate confidence. As a solution to the problem of uncertainty in yield estimation, the use of an on-site hydrodynamic method, called CORRTEX, has been proposed. The drawbacks compared to seismic methods are that CORRTEX requires pre-notification and full cooperation of the host country to the extent that foreign personnel and their equipment be allowed on the test site for each test. Furthermore, such hydrodynamic methods have limited application for monitoring a low-yield treaty and none for detecting clandestine testing. If the Soviet test site were seismically calibrated and advanced seismic methods were utilized, the uncertainty in seismic yield estimation could be reduced to a level comparable to CORRTEX and fufill the other functions as well. CORRTEX could be used to complement seismic methods by confirming the yields of the calibration shots.

Copies of the OTA report, "Seismic Verification of Nuclear Testing Treaties," are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325 (202) 783-3238. The GPO stock number is 052-003-01108-5; the price is $7.00. Copies of the report for congressional use *are available by calling 4-8996.*

Signal From Semipalatinsk



A 0.25 kt explosion at the Soviet test site recorded 3,800 km away at a seismic station in Norway

OTA REPORT BRIEF

June 1988

The Quality of Medical Care
Information for Consumers

OTA examined whether valid information on the quality of medical care could be developed and made available to the public to guide their choices of physicians and hospitals. Recent changes in how physicians and hospitals are paid have raised concerns that providers facing restricted budgets and low payment rates might skimp on services to the detriment of patients' health and that third-party payers will seek low-cost providers without sufficient attention to the quality of care. Advocates of better quality-of-care information expect that individuals and organizations would use improved consumer information to select hospitals and physicians, thereby exerting leverage on these providers to improve their performance.

After examining various ways to measure the quality of care, this OTA report concluded that several of the possible indicators can provide useful information to guide individuals and organizations in selecting physicians and hospitals. Although none of the possible measures can conclusively evaluate quality across the full range of medical care, several could be used to flag areas for further exploration. In evaluating a specific physician or hospital, OTA advises consumers to combine information from more than one indicator and to draw information from more than one year.

An accompanying table lists the potential indicators of quality that OTA evaluated and summarizes the strengths and weaknesses of each indicator (see reverse). Although OTA attempted to select the most promising indicators, the ones evaluated may not include the best measures for consumer use.

Of the indicators examined, formal disciplinary actions by State medical boards provide the most valid information about poor-quality physicians. In addition, the results of hospital accreditation, physicians' practicing in the area of their training, and patients' ratings of the interpersonal aspects of their care have good validity.

OTA places high priority on improving information on indicators that are already being disseminated and used, namely hospital mortality rates, adverse events, sanctions of the Department of Health and Human Services (HHS) based on recommendations by peer review organizations (PROs), and physician specialization. OTA also gives higher priority to efforts to identify and to improve the quality of physicians and hospitals whose performance falls below acceptable levels than to efforts to distinguish among good-quality providers.

In the course of evaluating the indicators, OTA identified several deficiencies in the field of quality assessment. Current techniques do not adequately adjust for patient and environmental factors than may influence patients' health and satisfaction independently of the quality of care. There is also a dearth of necessary data and a lack of uniform methods to code, collect, and report data. Further, although some information, most notably hospital mortality rates, is becoming available to the public, other relevant quality information, such as the results of hospital accreditation, is regularly compiled but not publicly available. Finally, how individuals and organizations use quality-of-care information and how information can most effectively be communicated remain largely unexplored. OTA developed policy options that Congress could adopt to improve quality assessment techniques, to ensure the quality of assessments, to improve the availability of required data, and to make quality-of-care information more available to the public.

Copies of the OTA report, "The Quality of Medical Care: Information for Consumers," are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325 (202) 783-3238. The GPO stock number is 052-003-01111-4; the price is $14.00. Copies of the report for **congressional use** *are available by calling 4-8996. Summaries of reports are available at no charge from the Office of Technology Assessment.*

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director.*

Summary of Key Findings on Quality-of-Care Indicators Evaluated by OTA

Strengths	Weaknesses
***Hospital mortality rates*:**	
• A substantial percentage of hospital deaths are preventable. • There has been some limited validation of the association between high mortality rates and poor performance. • Limited information is now publicly available.	• Techniques and clinical data to adjust for patients' risk are not available. • Using this indicator to measure quality may result in many false negatives and false positives. • Many lay and medical people lack sufficient knowledge to interpret the data.
***Adverse events, such as hospital-acquired infections*:**	
• A substantial percentage of adverse events are preventable. • Nosocomial infections have been partially validated as indicators of quality. • Infections of surgical wounds can be measured more reliably than all infections. • Two-stage systems of screening for adverse events and auditing medical records are already in widespread use in hospitals; the cost of implementing the use of adverse events as quality indicators would be low.	• Case finding of nosocomial infections is unreliable across hospitals. • No two-stage system, including the generic screens used by PROs, has been completely validated for evaluating quality across hospitals. • Using adverse events as quality indicators results in many false positives. • If use of adverse events as an indicator depends on providers' reporting adverse events, there is a high potential for gaming.
***Formal disciplinary actions by State medical boards against physicians*:**	
• The indicator gains credibility from the rigorous due process used. • Grounds for disciplinary actions extend beyond incompetence to felony, fraud, and impairment from drug abuse; if one accepts these grounds as relevant to quality, formal disciplinary actions are valid indicators of poor-quality physicians. • Information on formal disciplinary actions is already available.	• The precision of the grounds for disciplinary actions varies among State medical boards. • The indicator does not identify all poor-quality physicians; there are many false negatives. • Information on formal disciplinary actions is not well publicized in most States.
***PRO/HHS sanctions*:**	
• The PRO/HHS sanctioning process is a rigorous one. • Most grounds for sanctions relate to incompetence and inappropriate care.	• The PRO/HHS sanctioning process is new, evolving, and sometimes unclear. • The grounds for sanctions may relate to improper documentation by providers, which some may not deem to be related to the quality of care.
***Malpractice compensation*:**	
• Malpractice compensation indicates patient dissatisfaction. • Multiple jury awards justify attention.	• Single incidents of malpractice give little indication of technical quality. • Many factors unrelated to merits of a malpractice case affect its outcome.
***Evaluation of physicians' performance for a specific condition, such as hypertension*:**	
• Evaluations that combine explicit criteria and implicit judgment to review the medical care process, perhaps with patient outcomes to target review, hold promise as an indicator of quality, but are not well evaluated. • Evaluations across a range of medical conditions are promising, though not well evaluated.	• The validity of experts' criteria and standards has not been evaluated. • The generalizability of results to other settings and conditions is low. • Explicit review of physicians' performance raises the problem of false negatives, and implicit review raises the problem of the reliability of physicians' judgments.
***Volume of services in hospitals or performed by physicians*:**	
• Lower hospital volumes have been associated with higher rates of poor patient outcomes for certain services, mostly surgical. • Data on hospital volume are readily available from claims or hospital discharge abstracts; extra cost of data collection would be low.	• A relationship between volume and outcome has not been documented for services performed by physicians or for all services in hospitals. • Studies have not linked lower volume with poor performance. • Using volume of procedures as an indicator of quality would give providers an incentive to raise volume by relaxing standards of use.
***External standards and guidelines for scope of hospital services*:**	
• Standards and guidelines developed by external experts are a reasonable means for assessing minimum acceptable resources to manage certain conditions. • Some information on the indicator is collected and publicly available.	• The use of the indicator to measure quality has not been validated through process or outcome measures. • Information on the indicator is difficult to obtain.
***Physician specialization as measured by specialty board certification or by practicing in one's area of training*:**	
• Practicing in one's area of training has good validity as an indicator of the quality of technical aspects of care. • Information on the training of board-certified physicians is readily available.	• The association between practicing in one's area of training and providing better quality care is not generalizable across specialties or procedures. • Data on the training of non-board-certified physicians are not readily available. • Board certification is not a valid measure of quality.
***Patients' assessments of their care*:**	
• Patients' ratings are a valid indicator of interpersonal aspects of inpatient care and of physicians' ambulatory care. • Patients' assessments of technical aspects are promising, especially for physicians' ambulatory care, but have not been validated.	• Potential bias in assessments may result from patients' preferences or other characteristics. • Special surveys are required to collect data.

SOURCE: Office of Technology Assessment, 1988.

OTA REPORT BRIEF

June 1988

SDI: Technology, Survivability, and Software

The ultimate goal of the Strategic Defense Initiative (SDI) is to create defenses effective enough to "eliminate the military threat" of nuclear ballistic missiles and perhaps lead to an arms control agreement with the Soviets to eliminate the missiles themselves.

In mid-1987, the SDI Organization (SDIO) proposed taking the first steps toward developing and deploying a "phase one" ballistic missile defense (BMD) system in the mid-1990s.

Elements of a Phase One Strategic Defense System

- High-altitude satellites intended to detect and track ballistic missiles as they rise from their launchers
- A few thousand space-based interceptors (SBI) located on a few hundred satellite "garages" or "carrier vehicles" in low-earth orbit, intended to collide with missile boosters and warhead-carrying stages (called "post-boost vehicles")
- An infrared sensor system, either based on satellites or launched from the ground to high altitides during an attack, intended to detect and track missile warheads and decoys
- Several hundred ground-based interceptors intended to collide with missile warheads before they reentered the atmosphere

If phase one worked as planned, it might protect a substantial fraction of certain kinds of targets, such as ICBM silos. SDIO officials say that by reducing Soviet attack capabilities, this system would significantly enhance nuclear deterrence. Such a system might also offer general protection against small or accidental ballistic missile attacks.

The second and third phases of BMD development and deployment are less well defined. **These additional phases, however, would be essential to retain the capabilities of phase one in the face of future Soviet countermeasures and to extend BMD protection to urban and industrial targets.**

Possible Elements of Phases Two and Three

- Additional and improved space-based interceptors
- Ground-based interceptors designed to attack reentry vehicles inside the atmosphere
- "Interactive Discrimination" devices, perhaps neutral particle beam accelerators, to help distinguish between decoys and reentry vehicles disguised as decoys
- Directed-energy weapons, such as lasers to attack future missile boosters too fast to be reached by space-based interceptors

Principal OTA Findings

1. Many years of BMD research have led to impressive technical achievements, but **important technical issues remain to be resolved before the feasibility of reaching SDI goals can be determined.** The SDIO has initiated programs to address most, if not all, of these issues.

2. **The effectiveness of a first-phase BMD system in the mid-to-late 1990s would depend on several uncertain factors, including:**
   - affordably producing the system proposed;
   - deploying the system on the schedule proposed;
   - the effectiveness of likely countermeasures by the Soviets; and
   - the numbers of Soviet weapons that exist by then and the Soviet attack strategy.

3. The feasibility of modifying and adding to the phase one system to meet a changing Soviet threat in the year 2000 and beyond will remain uncertain for some time. Commitment in the early 1990s to full-scale development and deployment of a phase one system would occur before most of the experimental evidence on succeeding phases is complete. **Thus, a major issue will be whether Congress has enough confidence in the second and third phases of the system to commit to development and deployment of the first phase.**

4. **The survivability of a space-based BMD system is hard to estimate,** because it would depend on the

(over)

The Office of Technology Assessment (OTA) is an analytical arm of the U.S. Congress. OTA's basic function is to help legislators anticipate and plan for the positive and negative impacts of technological changes.
Address: OTA, U.S. Congress, Washington, DC 20510-8025. Phone: 202/224-9241. John H. Gibbons, *Director*.

specific weapons attacking it, the countermeasures against those weapons, the tactics used by each side, and the inevitable uncertainties of battle. For example, nuclear-armed anti-satellite weapons launched from the ground could seriously threaten a first-phase or second-phase BMD system.

5. **OTA found little analysis of space-based threats to BMD system survivability.** SDIO analyses have generally assumed that U.S. BMD technologies would remain superior to Soviet technologies. The SDIO and its contractors appear not to have studied seriously the possibility that the United States and the Soviet Union would both field comparable BMD systems. Moreover, the Soviets would not need to achieve BMD capabilities to begin to challenge U.S. control of, or even access to, space, since most BMD weapon technologies would have anti-satellite applications before they reached the levels of power and precision needed for BMD.

6. Because of the nature of software and past experience with large, complex software systems, **there may always be irresolvable questions about how dependable BMD system software would be.** Moreover, no adequate models exist for the development, production, testing, and maintenance of full-scale BMD software systems. The relatively slow rate of improvement in software engineering technology makes it appear to OTA unlikely that questions about BMD system software dependability would be resolved in the foreseeable future. SDIO officials, however, argue that software programs will be manageable and that simulation testing to permit sufficient confidence in the system will be possible.

7. There is broad agreement in the technical community that significant parts of the research being carried out under the aegis of the SDI are in the national interest. **Disagreement, however, centers on whether this research is best carried out within a program that is strongly oriented toward supporting an early 1990s BMD deployment decision and that includes system development as well as research elements.**

OTA prepared this report in response to a provision in the fiscal 1986 defense appropriations bill (Public Law 99-190).

Copies of the OTA report, "SDI: Technology, Survivability, and Software," are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325 (202) 783-3238. The GPO stock number is 052-003-01084-4; the price is $12.00. Copies of the report for **congressional use** *are available by calling 4-8996. Summaries of reports are available at no charge from the Office of Technology Assessment.*

88-743 0 - 88 - 2

TECHNOLOGY ASSESSMENT BOARD
MORRIS K. UDALL, ARIZONA, CHAIRMAN
TED STEVENS, ALASKA, VICE CHAIRMAN
ORRIN G. HATCH, UTAH
CHARLES E. GRASSLEY, IOWA
EDWARD M. KENNEDY, MASSACHUSETTS
ERNEST F. HOLLINGS, SOUTH CAROLINA
CLAIBORNE PELL, RHODE ISLAND
GEORGE E. BROWN, JR., CALIFORNIA
JOHN D. DINGELL, MICHIGAN
CLARENCE E. MILLER, OHIO
DON SUNDQUIST, TENNESSEE
AMO HOUGHTON, NEW YORK
JOHN H. GIBBONS

JOHN H. GIBBONS
DIRECTOR

Congress of the United States
OFFICE OF TECHNOLOGY ASSESSMENT
WASHINGTON, DC 20510-8025

April 28, 1988

TO: PRESS

FROM: OTA Press Office
Ellen Mika or Jean McDonald 202-228-6204

ABOUT: Press Conference on release of OTA Report:

New Developments in Biotechnology:
Field-Testing Engineered Organisms: Genetic and Ecological Issues

TIME: Wednesday, May 4, 1988, at 10:00 a.m.

PLACE: Room 2318 of the Rayburn House Office Building

Expected to attend are Rep. James H. Scheuer (D-NY), Chairman of the Subcommittee on Natural Resources, Agriculture Research and Environment of the House Science, Space and Technology Committee and Tom McMillen (D-MD), Member of that Committee. Representing OTA will be Luther Val Giddings, Project Director for the report.

Also, there will be a hearing of the Subcommittee on Natural Resources, Agriculture Research and Environment on the release of genetically engineered organisms in the environment, chaired by James H. Scheuer, on Thursday, May 5, 1988, at ~~9:30~~ 2:00 p.m. in Room 2318 of the Rayburn House Office Building.

Copies of the report are available from the OTA Press Office.

###

TECHNOLOGY ASSESSMENT BOARD
MORRIS K. UDALL, ARIZONA, CHAIRMAN
TED STEVENS, ALASKA, VICE CHAIRMAN
ORRIN G. HATCH, UTAH
CHARLES E. GRASSLEY, IOWA
EDWARD M. KENNEDY, MASSACHUSETTS
ERNEST F. HOLLINGS, SOUTH CAROLINA
CLAIBORNE PELL, RHODE ISLAND
GEORGE E. BROWN, JR., CALIFORNIA
JOHN D. DINGELL, MICHIGAN
CLARENCE E. MILLER, OHIO
DON SUNDQUIST, TENNESSEE
AMO HOUGHTON, NEW YORK
JOHN H. GIBBONS

JOHN H. GIBBONS
DIRECTOR

Congress of the United States
OFFICE OF TECHNOLOGY ASSESSMENT
WASHINGTON, DC 20510-8025

Hold for release until
Wednesday, *May 4, 1988, 10:00 a.m.*

For further information contact
Ellen Mika or Jean McDonald
(202)228-6204

The current review process for field-testing genetically engineered organisms is adequate to anticipate and prevent most potential problems, according to a report released today by Rep. James H. Scheuer, Chairman of the Subcommittee on Natural Resources, Agriculture Research, and Environment of the House Committee on Science, Space and Technology.

The report, prepared by the congressional Office of Technology Assessment (OTA), says that with adequate review, the small-scale field tests probable within the next few years are unlikely to result in any environmental problems that would be widespread or difficult to control.

Indeed, small-scale field tests may be the only way to resolve uncertainties about some commercial-scale uses of genetically engineered organisms, says OTA. If small-scale field tests do not identify areas of significant concern, there would be no scientific reasons not proceed with field tests or applications on a larger sale.

To date, approximately two dozen field tests of genetically engineered organisms have been carried out in at least 12 states and 4 foreign countries. In the future, field testing is expected to increase, OTA reports.

With recombinant DNA techniques, genetic material can be either added to or deleted from genetically-engineered organisms to make them serve a wide range of purposes: vaccines to protect humans and animals against diseases; agricultural crops with increased resistance to diseases, insect pests, or herbicides; crops with increased growth rates, improved nutritional qualities, better taste, or enhanced tolerance to environmental stresses; and microbes that can reduce crop losses to frost or improve environmental quality by degrading toxic wastes. (See attached table)

In some cases, such as pest control or toxic waste management, successful development of biotechnological tools could reduce dependence on older, more hazardous chemical technologies, OTA says. The application of biological approaches to many human activities could eventually prove to have less impact on the environment than traditional technologies.

MORE

Planned introductions of genetically engineered organisms into the environment are not, however, without potential risks, OTA says. Virtually any organism deliberately introduced into a new environment will have a small but real chance of surviving and multiplying. In some cases, an undesirable consequence might follow. Because even simple ecosystems are very complex, the precise prediction of such events and of their consequences, is difficult.

With further experience, the agencies regulating the release of engineered organisms, principally the Environmental Protection Agency and U. S. Department of Agriculture, should be able to make general conclusions about the safety of different types of introductions. They will probably be able to streamline the review process by assigning specific proposals to the appropriate level of review (e.g., low, medium and high), according to OTA.

OTA identified options for congressional action in three major areas of public policy related to this promising new application of biotechnology:

- criteria for regulatory review of planned introductions,
- administrative mechanisms for applying such review criteria,
- the research base supporting planned introductions.

OTA is a non-partisan analytical agency that serves the U.S. Congress. Its purpose is to aid Congress in dealing with the complex and often highly technical issues that increasingly confront our society.

Copies of the 142-page report, ***Field Testing Engineered Organisms: Genetic and Ecological Issues***, are available to the public at the U.S. Government Printing Office (GPO), Superintendent of Documents, Washington, D.C. 20402, phone (202) 783-3238. The GPO stock number is 052-003-01104-2 The price is $7.50. Copies for Congressional use may be obtained by calling OTA at 49241.

###

CONGRESSIONAL COMMENT

Rep. James H. Scheuer (D-NY), Chairman, Committee on Science, Space, and Technology, Subcommittee on Natural Resources, Agriculture Research and Environment:

"Biotechnology holds enormous promise for improving the quality of life in our country and in the developing world. New products developed through genetic manipulation can help clean up hazardous waste, improve medical care, reduce pollution from agricultural chemicals, and improve our nutrition.

"Yet commercialization of biotechnology has been hindered by a fear of the potential consequences of releasing genetically engineered organisms into the environment. The OTA report being released today provides the type of comprehensive, thoughtful, scientific review of this issue that has been sorely lacking. It gives us reassurance that we know enough to move ahead in bringing the benefits of biotechnology to the world and to protect the environment at the same time."

Senator Max Baucus(D-Montana):

"I support the rational development of biotechnology in the United States. We need to maintain our lead in this new technology. We need a regulatory system that will facilitate the development of safe biotechnologies into new products and industries, one that will protect the public but not tie up our scientists in a tangle of regulatory gibberish. The Office of Technology Assessment is to be commended for its comprehensive report on the scientific and policy issues that must be considered as we form our national policy on biotechnology."

Office of Technology Assessment - 4

Rep. John D. Dingell (D-Michigan), Chairman, House Energy and Commerce Committee and Member, Technology Assessment Board:

"Even as society is beginning to enjoy the benefits of the biomedical applications of biotechnology, we are still wrestling with the issues that surround those uses of biotechnology which involve the planned introduction into the environment of living, genetically-engineered organisms.

"As with any environmental intervention, the introduction of genetically-engineered organisms is not without potential risks. There is a perception however that organisms derived by the new recombinant DNA technologies could have completely unexpected and possibly harmful effects outside of the laboratory.

"The Office of Technology Assessment's report on *New Developments in Biotechnology: Field Testing Engineered Organisms: Genetic and Ecological Issues* addresses these perceptions and the concerns they raise, and offers guidance and options for how society should proceed. The OTA report shows us that we do not come to wrestle with the new scientific and social issues which biotechnology presents totally without intellectual, scientific and regulatory resources.

"I agree with the recommendations of the OTA report that the debate should not be stifled, but moved forward, fueled with new scientific data and experience gained by carefully managed field testing. It will be the responsibility of the Congress and the Administration to ensure that society, scientists, and industry have confidence in a scientifically-based, stream-lined and appropriate review process, based on guidelines and regulations that cover all the products and activities which need such review.

"We must proceed with biotechnology development and commercialization in such a way that the risks, where they exist, can be clearly identified and managed. Then we all stand to benefit soon from the applications of biotechnology to agriculture, toxic wastes clean-up, mining, and enhanced oil and mineral recovery."

Rep. Manuel Lujan, Jr. (R-NM), Ranking Republican Member, Committee on Science, Space, and Technology:

"This report, coupled with the previous OTA report on Public Perceptions of Biotechnology, is a valuable contribution to the debate over the safety and promise of biotechnology. It solidly states that our regulatory process is keeping pace with available technologies though appropriately calls for re-evaluation as the technology advances"

Some Representative Pending and Potential Environmental Applications of Genetically Engineered Organisms

MICRO-ORGANISMS

Bacteria as pesticides. "Ice-minus" bacteria to reduce frost damage to agricultural crops.

Bacteria carrying *Bacillus thuringiensis* toxin to reduce loss of corn crops to black cutworm.

Mycorrhizal fungi to increase plant growth rates by improving efficiency of root uptake of nutrients.

Plant symbionts. Nitrogen-fixing bacteria to increase nitrogen available to plants, and decrease need for fertilizers.

Toxic waste disposal. Bacteria engineered to enhance their existing abilities to degrade compounds found in sludge in waste treatment plants.

Bacteria engineered to enhance their abilities to degrade compounds in landfills, dumps, runoff deposits, and contaminated soils.

Heavy metal recovery. Engineered enhancements possible to several species of bacteria now used to recover metals from low-grade ores (e.g., copper and cobalt).

Pollution control. Possible increased utility of bacteria in purifying water supplies of phosphorus, ammonia, and other compounds.

Viruses as pesticides. Insect viruses with narrowed host specifity or increased virulence against specific agricultural insect pests, including cabbage looper, pine beauty moth, cutworms, and other pests.

Myxoma virus modified so as to restore its virulence against rabbits (which became resistant during early biocontrol efforts in Australia).

Viruses as vaccines. Vaccines against human diseases including:
- —hepatitis A and B
- —polio
- —herpes simplex (oral and genital)
- —malaria
- —acquired immunodeficiency syndrome
- —rabies
- —respiratory syncitial virus

Vaccines against animal diseases including:
- —swine pseudorabies
- —swine rotavirus
- —vesicular stomatitis (cattle)
- —foot and mouth disease (cattle)
- —bovine rotavirus
- —rabies (cattle, other mammals)
- —sheep foot rot
- —infectious bronchitis virus (chickens)
- —avian erythroblastosis
- —sindbis virus (sheep, cattle, chickens)

Multivalent vaccines. Vaccines possible for antigenically complex diseases such as:
- —malaria
- —sleeping sickness
- —schistosomiasis

PLANTS

Herbicide resistance or tolerance to:
- Glyphosate
- Atrazine
- Sulfonylurea (chlorosulfuron and sulfometuron)
- Imidazolinone
- Bromoxynil
- Phosphinotricin

Disease resistance to:
- Crown gall disease (tobacco)
- Tobacco mosaic virus (and related viruses)
- Potato leaf roll virus

Pest resistance
- BT-toxin-protected crops, including tobacco (principally as research tool) and tomato.
- Seeds with enhanced anti-feedant content to reduce losses to insects while in storage.

Enhanced tolerance to environmental factors, including:
- Salt
- Drought
- Temperature
- Heavy metals

Nitrogen-fixation enhancements
- Nonlegumes enhanced to fix nitrogen, independent of association with symbiotic bacteria.

Engineered marine algae
- Algae enhanced to increase production of such compounds as B-carotene and agar, or to enhance ability to sequester heavy metals (e.g., gold and cobalt) from seawater.

Forestry
- Trees engineered to be resistant to disease or herbicides, to grow faster, or to be more tolerant to environmental stresses.

ANIMALS

Livestock and poultry
- Livestock species engineered to enhance weight gain or growth rates, reproductive performance, disease resistance, or coat characteristics.
- Livestock animals engineered to function as producers for pharmaceutical drugs, especially of mammalian compounds that require post-synthesis modifications in the cell.

Fish
- Triploid salmon produced by heat shock for use as game fish in lakes and streams.
- Fish with enhanced growth rates, cold tolerance, or disease resistance for use in aquaculture.
- Triploid grass carp for use as aquatic weed control agents.

SOURCE: Office of Technology Assessment, 1986.

TECHNOLOGY ASSESSMENT BOARD
MORRIS K. UDALL, ARIZONA, CHAIRMAN
TED STEVENS, ALASKA, VICE CHAIRMAN
ORRIN G. HATCH, UTAH
EDWARD M. KENNEDY, MASSACHUSETTS
ERNEST F. HOLLINGS, SOUTH CAROLINA
CLAIBORNE PELL, RHODE ISLAND
CHARLES E. GRASSLEY, IOWA
GEORGE E. BROWN, JR., CALIFORNIA
JOHN D. DINGELL, MICHIGAN
CLARENCE E. MILLER, OHIO
DON SUNDQUIST, TENNESSEE
AMO HOUGHTON, JR., NEW YORK
JOHN H. GIBBONS

JOHN H. GIBBONS
DIRECTOR

Congress of the United States
OFFICE OF TECHNOLOGY ASSESSMENT
WASHINGTON, DC 20510-8025

OTA Fact Sheet

The Office of Technology Assessment (OTA) is a nonpartisan analytical support agency created in 1972 to serve the Congress (Public Law 92-484). OTA's job is to analyze complex issues involving science and technology for both Senate and House Committees. It clarifies the range of policy options on a given issue and the potential physical, biological, economic, social, and political implications of each of these options. OTA typically delivers 20 or more major analyses every year.

A 12-member bipartisan Congressional Board—six Senators and six Representatives—governs OTA. Representative Morris K. Udall (D-Ariz.) is Chairman and Senator Ted Stevens (R-Alaska) is Vice Chairman for the 99th Congress. These posts alternate between the Senate and House with each Congress.

The Board appoints the OTA Director, who is chief executive officer and a nonvoting Board member. Dr. John H. Gibbons, nationally known scientist, has served as Director since June 1979.

The Congressional Board is assisted by an Advisory Council comprised of 10 distinguished individuals from the public and private sector and, ex officio, the Comptroller General of the United States and the Director of the Congressional Research Service of the Library of Congress.

The Chairman of the Advisory Council is Dr. William J. Perry, managing partner, H&Q Technology Partners.

OTA has three assessment divisions, each headed by an Assistant Director: Energy, Materials, and International Security, under Lionel S. Johns; Health and Life Sciences, under Roger Herdman; and Science, Information, and Natural Resources, under John P. Andelin, Jr. Within these divisions are nine general program areas: energy and materials; international security and commerce; industry, technology, and employment; biological applications; food and renewable resources; health; communication and information technologies; oceans and environment; and science, education, and transportation.

OTA has an in-house staff of about 100 professionals whose skills span the fields of physical, life, political, and social sciences; mathematics; engineering; law; and medicine. Throughout each project, OTA uses advisory panels of experts and representatives of major parties-at-interest as a way of ensuring that reports are nonduplicative, objective, fair, and authoritative. OTA draws extensively on the broad spectrum of resources throughout the private sector to ensure the quality and completeness of its work.

OTA reports are available to the public through the U.S. Government Printing Office and the National Technical Information Service. Many of OTA's reports have also been reprinted by commercial publishers, and a few translated and printed in foreign languages.

Revised March 1987

Mr. SCHEUER. Congresswoman Schneider.

Miss SCHNEIDER. Thank you, Mr. Chairman.

I am interested from an international perspective. How do we compare as a nation in terms of our degree of research and in terms of our degree of regulatory infrastructures?

Dr. GIDDINGS. It's a very complex picture. Some foreign countries regulate much more harshly than we do.

Miss SCHNEIDER. Can you use some specific countries as examples, please?

Dr. GIDDINGS. If I'm correct in my understanding, I believe that the current regulations, for example, in Japan are based on the NIH guidelines of about a decade ago, which puts us in a considerably more liberal position as regards regulation.

Great Britain, on the other hand, with their Advisory Committee on Genetic Manipulation, they do go through, as we do now, essentially a case-by-case review of proposed applications for permission to field test. But they may be a little more flexible. That may be primarily because they have a single agency involved. There are no potential problems of overlapping jurisdiction or competing responsibilities, the kinds of problems that the BSCC was established here in order to take care of.

But it's quite a complicated picture internationally in terms of regulation. Some countries do not have any regulation on the books at all, but most of them are not doing a whole lot of research in this area.

We do have a discussion of this in—a brief discussion of some of this in Chapter 3.

As far as research goes, there are a couple of foreign countries that are right up there in the forefront. Belgium has at least one company in plant genetics that is doing world class work, and it would certainly be difficult to argue that anybody else was ahead of them.

There are some people working, for example, on making certain insect viruses useful as vectors for pest control, primarily at Oxford in England, and they are certainly world leaders. But the same kind of research on insect viruses is being done in a couple of different companies and academic research groups here in the U.S., and there is much—very good plant research going on here in the U.S., although there is obviously a need for more in certain areas.

I think that overall it's probably still a very safe statement to make that no one is ahead of us. We're in the forefront. And certainly no other country has the kind of breadth of research that we do over the broad range of possible areas that are involved.

Miss SCHNEIDER. To what degree have you analyzed the federal commitment to research in this field?

Dr. GIDDINGS. Well, we had limited resources to devote to this study, and we really wanted to look at that question in detail. We do have—the next study in this series does explore in some depth the U.S. investment in biotechnology, and that will be released probably next month or the month after, depending on how we get through the publication queue.

In this study, we did not look at it in great detail.

Miss SCHNEIDER. Okay. I don't have any further questions, Mr. Chairman.

Mr. SCHEUER. Thank you, Congresswoman Schneider.

Several months ago, a scientist in Montana conducted an unauthorized field test involving the Dutch elm disease, and he claimed that it was unclear, that his status was unclear, from the policy, whatever policy there was that he interpreted, regarding these kinds of experiments.

In this study, you interviewed scientists from industry and from academe. Do you sense that the scientific community, both in industry and in academe, understands what is expected from them under the federal regulations as they now exist on biotechnology?

Dr. GIDDINGS. I think at one level there is a certain amount of uncertainty. You know, many regulations are still in the temporary stage and so on and so forth. But it is my impression that most scientists have a pretty clear understanding that if they're working with an engineered plant, generally they go to USDA. With an engineered microbe, generally they go to EPA. And I don't sense the kind of large-scale, you know, broad-ranging confusion that some people assert exists.

My sample on this particular question may not be representative. The particular example that you referred to with Gary Strobel at Montana State University, there were some particular uncertainties that Dr. Strobel was faced with. He apparently had gotten some information which he misunderstood from some people, who purported to be informed on the regulatory issues quite well. It's a very complex situation that has been looked at by a hearing in the Senate that Senator Baucus convened last fall.

But generally to give you a brief answer, I don't see a very great deal of confusion out there. The broad spectrum of requirements that are in place now seem to be fairly clear to most people that we've talked with.

Mr. SCHEUER. Do you think that industry scientists and scientists in the teaching professions, in academe, feel they have a pretty clear roadmap and understand pretty well the constraints under which they must function?

Dr. GIDDINGS. I believe that's probably the case. They, of course, can speak for themselves far better than I can. I think they would be happier, many people would be happier, if the regulations involved were not 50 pages of fine print in the Federal Register, you know, but in spite of that, they generally seem to have a fairly clear idea of what's required of them.

Mr. SCHEUER. Of course, there's a real need for top quality research aimed at developing risk assessment methodologies for genetically-engineered organisms.

Do you think that should be best be done in the public sector? Must it be done in the public sector, or can we rely on the private sector to do that also?

Dr. GIDDINGS. I think probably the best approach would involve a mixture of both. There are certain kinds of research that are much more applied in nature that might best be funded by the public sector—I'm sorry—by the private sector.

But then again, you know, on some of these kinds of questions that involve understanding ecosystems and their function and relationsips between their components, a lot of this involves very fundamental and basic research, which will have applications when

it's developed, you know, but this is precisely the kind of basic research, basic information, fundamental knowledge, that the Federal Government in the past has viewed as its responsibility to help stimulate and encourage.

Mr. SCHEUER. Well, what do you think now? Is basic theoretical research properly the province of the federal agencies, or could this well be funded in the universities, in academe, or could we engage in some kind of cooperative funding effort to do some of this basic theoretical research in the private sector?

Dr. GIDDINGS. I kind of feel like I'm being put on the spot. My opinion, I'm not sure—

Mr. SCHEUER. That's the purpose of these hearings, Doctor.

Dr. GIDDINGS. I understand.

[Laughter.]

Dr. GIDDINGS. I might point out that my own personal opinion has got not much validity here. Basic research of the type we're referring to, however, has been funded extensively by the Federal Government in the past, primarily through NSF and NIH.

In particular in this area, in the course of our study, we identified a compelling need for some interdisciplinary kinds of research, both basic research and in terms of manpower training, personnel training, and that kind of research is particularly unlikely to be picked up by the private sector and therefore may be an especially appropriate candidate for federal support.

The people from NIH, I think, if they would wish to talk about this later on today, might have particularly worthwhile comments on that.

Mr. SCHEUER. Well, we're going to have—it's very much in the interest of our country for a great deal more basic theoretical research to be done.

Now there's a heck of a lot of talent, there's a heck of a lot of genius in the private sector, in the chemical industry for example, which is not exactly what we're talking about, but there are extraordinarily talented engineers and scientists and chemists at DuPont and other companies that produce the wide variety of chemicals that have produced the so-called "better living through chemistry" that have given us a lot of problems under the law of unpredicted consequences that we never envisioned—polluted groundwater and toxic waste dumps and all that—and my feeling has always been that we ought to harness the genius that created these substances to help us produce the answers and not leave it to government to produce the answers to the problems that have been created by the admittedly brilliant experts in the private sector who created these substances, which, of course, nobody at that time anticipated would come back to plague us as they have.

Can you think of any formula by which we can harness the private sector to do basic theoretical research, perhaps some kind of joint funding, and thereby tapping that vast reservoir of terrific, extraordinary talent and not leaving it all to the government agencies.

Dr. GIDDINGS. Yes. I think, Congressman, that NSF is exploring some initiatives in this area right now with some of the cooperative arrangements that they've tried to stimulate between industry and universities. I know that there are such companies as Monsanto

that have entered into cooperative research arrangements, for example, with scientists in the Biology Department at Washington University in St. Louis to pursue both fundamental and applied research in this area. There are some excellent collaborations going on.

Monsanto is also engaged in a collaborative arrangement with scientists at Clemson where they are now conducting a piece of applied research which is very basic in many of its aspects.

Mr. SCHEUER. It's comes close to being basic research?

Dr. GIDDINGS. Yes. Some of this—

Mr. SCHEUER. It's both.

Dr. GIDDINGS. It's hard to draw a line between some of this kind of work. There are many elements of microbial ecology which, when we understand the basics—

Mr. SCHEUER. Micro?

Dr. GIDDINGS. Microbial ecology, which, when we understand the basics of that, we can immediately see some applications of it.

Monsanto and Clemson right now are in Month 5.0 of an 18-month study that involves investigating the way engineered microbes with particular DNA sequences, the way they survive in association with plants and how far they migrate when they're in the soil, how long they last, things like that.

There are a number of things that are going on that I think can be encouraged by the Federal Government. I don't think this is at all an area where the Federal Government should pick up the entire tab, but there is a role for federal funding of basic research in this area of the kind that private industry would not—

Mr. SCHEUER. Federal funding of basic research, some of which might be carried on in the private sector.

Dr. GIDDINGS. Exactly.

Mr. SCHEUER. With perhaps a federal contribution to its funding.

Dr. GIDDINGS. Right.

Mr. SCHEUER. Partial funding by the private sector and partial by the Federal Government.

Dr. GIDDINGS. Yes. I believe some of these sorts of questions will be examined in more detail in an upcoming OTA study that I alluded to on U.S. investment in biotechnology. I'm really not the best one to ask about the details of this kind of funding sorts of arrangements.

Mr. SCHEUER. Well, thank you very, very much, Dr. Giddings.

We're going off the record. We're going to make you the beneficiary of an early release program now.

[Laughter.]

Dr. GIDDINGS. Thank you very much.

Mr. SCHEUER. Thank you very much for your very excellent testimony.

We're now within about three or four minutes of another roll call vote, so I think we'll suspend for about fifteen minutes and get over there. It will probably be on by the time we get there, and then we'll come right back, okay?

So we'll suspend about fifteen minutes.

[Recess.]

Miss SCHNEIDER [PRESIDING]. Congressman Scheuer is not back with us yet. I'm sure that his arrival is imminent, but considering

we have so many interruptions with the votes, I think it only appropriate that we do move ahead.

Let me welcome Dr. James Wyngaarden, Biotechnology Science Coordinating Committee and also the Director of the National Institutes of Health; Dr. Jack Moore, the Assistant Administrator, Office of Pesticides and Toxic Substances; and Dr. Kenneth Gilles, Assistant Secretary for Marketing and Inspection Services of the U.S. Department of Agriculture.

Welcome, gentlemen. Each of you have had an enormous amount of experience in this field, so we are looking forward to hearing your testimony.

Dr. Wyngaarden, would you please begin?

And let me also mention that your statements will be included in the record in their entirety, but if you would like to summarize them, that would be terrific.

Thank you.

STATEMENTS OF DR. JAMES WYNGAARDEN, BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE AND DIRECTOR, NATIONAL INSTITUTES OF HEALTH; DR. JOHN A. MOORE, ASSISTANT ADMINISTRATOR, OFFICE OF PESTICIDES AND TOXIC SUBSTANCES, ENVIRONMENTAL PROTECTION AGENCY; AND DR. KENNETH GILLES, ASSISTANT SECRETARY FOR MARKETING AND INSPECTION SERVICES, U.S. DEPARTMENT OF AGRICULTURE

Dr. WYNGAARDEN. Thank you, Madam Chairwoman. I will do that. I've collected some comments for highlighting, and I'd like to present those.

My first comments have to do with the Coordinated Framework for the Regulation of Biotechnology, the so-called BSCC.

In April of 1984, the Cabinet Council Working Group on Biotechnology was established in the Office of Science and Technology Policy to study and coordinate the federal regulatory policy for the products of biotechnology. It was directed to review the federal regulatory rules and procedures relating to biotechnology including the function of the NIH Recombinant DNA Advisory Committee and its role in biotechnology commercialization and safety regulation.

As a result, a proposal for a Coordinated Framework for regulation of biotechnology was published in the Federal Register in December 1984 and a final document published in June 1986. This document sets forth the overall policies of federal agencies involved in the oversight of biotechnology research and products and outlines the general policy framework within which regulatory decisions will be made.

As the oversight process evolved, the Biotechnology Science Coordinating Committee was established on October 30, 1985. The BSCC is a committee of the Federal Coordinating Council for Science, Engineering, and Technology, which is a statutory interagency coordinating mechanism within the Office of Science and Technology Policy in the Executive Office of the President.

The BSCC was established to provide an opportunity for interagency science policy coordination and guidance and the exchange

of information regarding the scientific aspects of biotechnology applications submitted to federal research and regulatory agencies for approval; promote consistency in the development of federal agencies' review procedures and assessments; and to facilitate continuing cooperation among federal agencies on emerging scientific issues and identify gaps in scientific knowledge.

The charter authorizes the BSCC to receive information regarding the scientific aspects of biotechnology applications submitted to federal research and regulatory agencies for approval, to conduct analyses of broad scientific issues that extend beyond those of any one agency, and to develop generic scientific recommendations that can be applied to similar recurring applications.

BSCC is authorized to convene workshops and coordinate special studies related to scientific issues in biotechnology. The committee holds periodic public meetings.

The BSCC is composed of senior representatives of the Department of Agriculture, the Department of Health and Human Services, the Environmental Protection Agency, and the National Science Foundation. From its inception through 1987, the chairman of the BSCC was Dr. David Kingsbury, Assistant Director of the NSF for Biological, Behavioral, and Social Sciences. Under his leadership, the BSCC evaluated a variety of issues relating to the coordination and oversight of emerging biotechnology. In particular, the committee considered the appropriateness of unified federal guidelines, the adequacy of greenhouse/release guidelines, biotechnology activities in the international arena, and proposed changes to existing guidelines and regulations. Considerable effort was also spent in reviewing documents for a proposed Coordinated Framework for the regulation of biotechnology.

The committee was rechartered in October of 1987, and the NIH Director was appointed Chair in November of that year.

On February 17th of this year, I chaired the first meeting of the rechartered BSCC. A number of topics were discussed including a follow-up to the National Academy of Science' report, "Introduction of Recombinant DNA- Engineered Organisms into the Environment: Key Issues;" the establishment and role of the Agricultural Biotechnology Research Advisory Committee; an NSF report on biotechnology research and development activities in industry; and a USDA proposed rule on the control of confidential business information involving agricultural research and related responsibilities.

At its March 25 meeting, the BSCC discussed proposed revised EPA biotechnology regulations; the March '88 meeting of the Agricultural Biotechnology Research Advisory Committee; an update of activities of the Risk Assessment Subcommittee; and a draft pamphlet on biotechnology regulations prepared by the Industrial Biotechnology Association.

The BSCC is authorized to form subcommittees and working groups. Currently a Risk Assessment Subcommittee is undertaking an in-depth survey of federal agencies to determine their procedures for conducting risk assessments of biotechnology products. The committee plans to submit a report of its findings to the BSCC.

The BSCC is also considering currently a proposal received from the National Academy of Sciences to assess what scientific knowl-

edge should underlie the federal oversight and regulation of the environmental use of genetically-engineered microorganisms.

In the international arena, at a meeting last month of national experts on safety and biotechnology sponsored by the Organization for Economic Cooperation and Development in Paris, progress was made toward developing "Good Developmental Practices"(GDP) criteria for limited-scale controlled field trials of organisms. GDP would refer to low or negligible-risk organisms and the practices appropriate for their field testing. A draft U.S. document entitled "GDP General Principles" will be the starting point for this effort for which a working group has been appointed for this year.

Finally, I would like to mention a few points related to the activities of the NIH RAC. In this earliest rendition of the RAC Guidelines, there were a number of prohibited practices that were placed in a section entitled "Experiments that Require RAC Review and NIH and IBC Approval Before Initiation." Included in that category was deliberate release into the environment of any organism containing recombinant DNA.

The 1983 revision of the guidelines incorporated new procedures for approval of field testing under certain specified conditions of certain plants modified by recombinant DNA. These now require review by the RAC Plant Working Group, but no longer by the full RAC prior to approval by NIH.

And finally in August 1987, the following provision was added to the guidelines, and this reflects the input of the Coordinated Framework of BSCC:

"Any recombinant DNA experiment, which according to these guidelines requires approval by the NIH, may be sent by the submitter to the NIH or to another federal agency that has jurisdiction for review and approval. Once approval or other applicable clearances have been obtained from a federal agency other than the NIH, whether the experiment is referred to that agency by the NIH or sent directly there by the submitter, the experiment may proceed without the necessity of NIH review or approval. However, any experiment that involves the administration of gene therapy to human subjects may not proceed without prior review by the NIH Recombinant DNA Advisory Committee and NIH approval."

With these new procedures, it is anticipated that most experiments involving release into the environment of organisms containing recombinant DNA will fall under the jurisdiction of other federal agencies rather than NIH.

Thank you very much. The rest I'll submit for the record.

[The prepared statement of Dr. James Wyngaarden follows:]

For Release Upon Delivery

STATEMENT BY

JAMES B. WYNGAARDEN, M.D.

DIRECTOR

NATIONAL INSTITUTES OF HEALTH

AND CHAIRMAN

BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE

BEFORE THE

HOUSE SCIENCE, SPACE, AND TECHNOLOGY

SUBCOMMITTEE

ON NATURAL RESOURCES,

AGRICULTURE RESEARCH AND ENVIRONMENT

MAY 5, 1988

Mr. Chairman and Members of the Subcommittee:

I am pleased to appear before you to discuss the role of several government groups in the oversight of biotechnology. This is an area in which oversight by the National Institutes of Health (NIH) Recombinant DNA Advisory Committee and several interagency committees has proved to be most effective.

Coordinated Framework for Regulation of Biotechnology

In April 1984, the Cabinet Council Working Group on Biotechnology was established in the Office of Science and Technology Policy to study and coordinate the Federal regulatory policy for the products of biotechnology. It was directed to review the Federal regulatory rules and procedures relating to biotechnology, including the function of the NIH Recombinant DNA Advisory Committee and its role in biotechnology commercialization and safety regulation. As a result, a "Proposal for a Coordinated Framework for Regulation of Biotechnology" was published in the Federal Register of December 31, 1984 and a final document was published on June 26, 1988. This document sets forth the overall policies of Federal agencies involved in the oversight of biotechnology research and products and outlines the general policy framework within which regulatory decisions will be made.

Biotechnology Science Coordinating Committee

As the oversight process evolved, the Biotechnology Science Coordinating Committee (BSCC) was established on October 30, 1985. The BSCC is a committee

of the Federal Coordinating Council for Science, Engineering and Technology, which is a statutory interagency coordinating mechanism within the Office of Science and Technology Policy, Executive Office of the President.

The BSCC was established (1) to provide an opportunity for interagency science policy coordination and guidance and for the exchange of information regarding the scientific aspects of biotechnology applications submitted to Federal research and regulatory agencies for approval; (2) promote consistency in the development of Federal agencies' review procedures and assessments; (3) facilitate continuing cooperation among Federal agencies on emerging scientific issues; and (4) identify gaps in scientific knowledge.

The charter authorizes the BSCC to receive information regarding the scientific aspects of biotechnology applications submitted to Federal research and regulatory agencies for approval, to conduct analysis of broad scientific issues that extend beyond those of any one agency, and to develop generic scientific recommendations that can be applied to similar, recurring applications. The BSCC is authorized to convene workshops and coordinate special studies related to scientific issues in biotechnology. The committee holds periodic public meetings.

The BSCC is composed of senior representatives of the Department of Agriculture (USDA), the Department of Health and Human Services, the Environmental Protection Agency (EPA), and the National Science Foundation (NSF). From its inception through 1987, the chairman of the BSCC was Dr. David Kingsbury, Assistant Director of the NSF for Biological, Behavioral and Social Sciences.

Under Dr. Kingsbury's leadership the BSCC evaluated a variety of issues related to the coordination and oversight of emerging biotechnology. In particular, the Committee considered the appropriateness of unified Federal guidelines, the adequacy of greenhouse/release guidelines, biotechnology activities in the international arena, and proposed changes to existing guidelines and regulations. Considerable effort was also spent in reviewing documents for a proposed coordinated framework for the regulation of biotechnology.

The committee was rechartered in October 1987 and the NIH Director was appointed chair on November 23, 1987.

On February 17 of this year, I chaired the first meeting of the rechartered BSCC. A number of topics were discussed including a follow-up to the National Academy of Sciences (NAS) report, "Introduction of Recombinant DNA-Engineered Organisms into the Environment: Key Issues"; the establishment and role of the Agricultural Biotechnology Research Advisory Committee; an NSF report on biotechnology research and development activities in industry, and a USDA proposed rule on control of confidential business information involving agricultural research and related responsibilities.

At its March 25 meeting, the BSCC discussed proposed revised EPA biotechnology regulations; the March 23-24, 1988 meeting of the Agricultural Biotechnology Research Advisory Committee; an update on activities of the Risk Assessment Subcommittee; and a draft pamphlet on biotechnology regulations prepared by the Industrial Biotechnology Association.

The BSCC is authorized to form subcommittees and working groups. Currently a Risk Assessment Subcommittee is undertaking an in-depth survey of Federal agencies to determine their procedures for conducting risk assessments of biotechnology products. The subcommittee plans to submit a report of its findings to the BSCC.

The BSCC is also considering an in-depth study to assess what scientific knowledge should underlie the Federal oversight and regulation of the environmental use of genetically engineered microorganisms.

In the international arena, at a meeting last month of national experts on safety in biotechnology sponsored by the Organization for Economic Cooperation and Development progress was made towards developing "Good Developmental Practices" (GDP) criteria for limited scale controlled field trials of organisms. GDP would refer to low or negligible risk organisms and the practices appropriate for their field testing. A draft U.S. document, "GDP General Principles," will be the starting point for this effort.

Historical Review of Guidelines for Recombinant DNA Research

The need for oversight of biotechnology was foreseen in 1973 in response to the concern of scientists involved in the development of recombinant DNA techniques. At their request, NAS formed a Committee on Recombinant DNA Molecules. This committee recommended that the Director, NIH, establish a committee (now the Recombinant DNA Advisory Committee) to (a) oversee a program to evaluate hypothetical risks, (b) develop procedures to minimize the spread of recombinant DNA molecules, and (c) recommend guidelines to be followed by

investigators. In addition, the report recommended that an international meeting be convened to review progress and discuss ways to deal with potential hazards.

The scientists at that meeting concluded that most recombinant DNA experiments should proceed, provided that appropriate containment is utilized. The conference report made general recommendations for matching levels of containment with levels of hypothetical hazard for various types of experiments. The NIH was then called upon to translate these broadly based recommendations into detailed guidelines for research. NIH was thus the first Federal agency to exercise oversight of experiments involving recombinant DNA. The original NIH Guidelines were issued in 1976 and have been revised periodically since then.

Release Into the Environment

I would like to summarize the evolution of the NIH Guidelines with regard to release into the environment of organisms containing recombinant DNA molecules. The original version of the Guidelines specified that five classes of experiments were "not to be initiated at the present time." Among these were experiments involving the deliberate release into the environment of any organism containing a recombinant DNA molecule. This prohibition was retained in the first revision, although exceptions to prohibited experiments were now permitted. By April 1982, however, experiments that were previously prohibited were placed in a new section entitled "Experiments that Require RAC Review and NIH and IBC (Institutional Biosafety Committee) Approval Before Initiation."

Included again in this category was deliberate release into the environment of any organism containing recombinant DNA. The procedures for approval remained the same, but use of the term "prohibited" was dropped.

The 1983 revision of the Guidelines incorporated new procedures for approval of field testing under certain specified conditions of certain plants modified by recombinant DNA techniques; these now require review by the RAC Plant Working Group, but no longer by the full RAC, prior to approval by NIH.

In August 1987, the following provision was added to the Guidelines:

> "Any recombinant DNA experiment which according to these Guidelines requires approval by the National Institutes of Health (NIH), may be sent by the submitter to the NIH or to another Federal agency that has jurisdiction for review and approval. Once approval, or other applicable clearances, has been obtained from a Federal agency other than the NIH (whether the experiment is referred to that agency by the NIH, or sent directly there by the submitter), the experiment may proceed without the necessity for NIH review or approval. However, any experiment that involves the administration of gene therapy to human subjects (see Section III-A-4 of the Guidelines) may not proceed without prior review by the NIH Recombinant DNA Advisory Committee and NIH approval."

It is anticipated that most experiments involving release into the environment of organisms containing recombinant DNA will fall under the jurisdiction of other Federal agencies.

The Role of Other Federal Agencies

The responsibilities of FDA, USDA, and EPA are determined by statute and are generally based on characteristics or uses of the end products.

The Toxic Substances Control Act (TSCA) authorizes the Environmental Protection Agency to acquire information on and regulate chemical substances and mixtures of chemical substances. The statute gives EPA jurisdiction over the manufacturing, processing, distribution, use, and disposal of chemical substances. TSCA's applicability to the regulation of microbial biotechnology products is based on the agency's interpretation that microbes are chemical substances under TSCA. The Federal Insecticide, Fungicide, and Rodenticide Act establishes authority over the distribution, sale, and use of all pesticide products, including microbial pesticides. Generally a pesticide must be registered with EPA in order to be distributed, sold, or used in the United States.

The United States Department of Agriculture (USDA) has the responsibility to assure the safety of agricultural research in the same way as NIH assures the safety of biomedical research. The USDA has broad regulatory authority to protect U.S. agriculture against threats to animal health and to prevent the introduction and dissemination of plant pests and noxious weeds. This authority is applied to the regulation of animal, veterinary biological products, plants, and microorganisms through animal quarantine laws, the Virus Serum Toxin Act, the Federal Plant Pest Act, and the Plant Quarantine Act.

The FDA's review of products, including those that employ specialized biotechnological techniques, is conducted in the light of the intended use of a product on a case- by-case basis. FDA regulates new drugs and biologics under the Food, Drug, and Cosmetic Act (FDCA). Manufacturers of new drugs and biologics must operate in conformance with current good manufacturing practice regulations. For new medical devices, including diagnostic devices for human use, either a premarket approval application or reclassification petition is required. The FDCA requires FDA preclearance of food additives, including those prepared using biotechnology.

Mr. Chairman, that concludes my prepared statement. I would be pleased to answer any questions you may have.

Mr. SCHEUER. Thank you, Dr. Wyngaarden.

Dr. Moore?

Dr. MOORE. Thank you, Mr. Chairman.

I'd just like to make a few brief summary remarks extracted from my testimony.

Mr. SCHEUER. We have about fifteen minutes left. So if you could take three or four minutes and Dr. Gilles take three or four minutes, we'll have six or seven minutes for questions, and I deeply apologize for the time crunch.

Dr. MOORE. Mr. Chairman, as I think you know, EPA proposes to regulate biotechnology under two statutes, the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Toxic Substances Control Act (TSCA). Under those two statutes to date, EPA has received 16 applications for review under one of the statutes and 12 under the other. Under both of those statutes, we have approved environmental releases for four under the Toxic Substances Control Act, and we have approved nine requests for field experiments involving release of organisms under the FIFRA statute. The other organisms are still under review, and in one instance, the original request was withdrawn. In all instances, we have usually had to request additional information in order to make a determined judgment.

We have a review process which is similar under both statutes and I might say tracks very closely with that of sister agencies. It's a case-by-case approach. The EPA staff reviews the information, comes up with an initial scientific position. Interagency work group comment is then solicited. In some cases, we solicit independent peer review by an outside group of experts on the agency interpretation and proposed action. We also allow several opportunities for public comment prior to that final decision having been implemented.

Several of these approved experiments have been conducted or are currently being conducted, and although it's probably premature, the results of those experiments have to date comported very nicely with the expected expert opinion based on the reviews prior to the experiments having been approved.

Thank you.

[The prepared statement of Dr. John A. Moore follows:]

STATEMENT OF
JOHN A. MOORE
ASSISTANT ADMINISTRATOR FOR
PESTICIDES AND TOXIC SUBSTANCES
U.S. ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
COMMITTEE ON SCIENCE, SPACE AND TECHNOLOGY
SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURAL
RESEARCH AND ENVIRONMENT
U.S. HOUSE OF REPRESENTATIVES

MAY 5, 1988

I am pleased to have the opportunity to appear before the Subcommittee on Natural Resources, Agricultural Research and Environment today to discuss the U.S. Environmental Protection Agency's (EPA) regulation of products derived using biotechnology. The responsible regulation of these products is one of my highest priorities and I fully recognize that it is essential that the public have confidence that the process we have established protects public health and the environment. It is also important that the scientific and regulated communities believe that our review process is credible, equitable, and sound, while allowing the development and commercialization of biotechnology products to proceed in a reasonable and timely manner. I will describe how EPA's implementation of its statutory responsibilities under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Toxic Substances Control Act (TSCA) provides reasonable and responsible regulation, and review the last 20 months of experience with regulation of biotechnology products under the Coordinated Framework for Biotechnology. Attached as Appendices to this testimony are tables describing briefly EPA's

reviews to date under these two statutes (Appendix A) and responses to your written questions (Appendix B).

As you know, EPA is one of several Federal agencies involved in regulating biotechnology products. To present the context in which EPA regulates products of biotechnology, I would like to take a moment to describe the Federal Coordinated Framework for the regulation of biotechnology and the philosophy which led to its adoption.

In 1984, the U.S. government, recognizing its responsibility to address issues raised by the use of biotechnology, formed an interagency working group under the White House Cabinet Council on Natural Resources and the Environment. This group examined existing laws and concluded that, for the most part, these laws would adequately address regulatory needs in biotechnology.

The federal approach to regulating biotechnology recognizes that biotechnology encompasses a large and varied collection of techniques and activities, and that the products potentially resulting from this technology will cover a wide spectrum of uses. The Coordinated Framework provides that biotechnology products will be regulated in the U.S. as are products of other technologies, i.e., by the various regulatory agencies on the basis of use.

Thus, many agricultural uses of microorganisms, plants and animals are regulated by the U.S. Department of Agriculture (USDA) under a variety of statutory authorities; foods, drugs and related items are regulated by the Food and Drug Administration (FDA)

under its authorities; microorganisms used as pesticides are regulated by EPA under FIFRA, and commercial uses of microorganisms not covered by other existing authorities are regulated by EPA under TSCA. Examples of the types of uses covered by TSCA include microorganisms used in metal mining, degrading wastes, conversion of biomass for energy, production of proteins and enzymes for non-pharmaceutical purposes, and non-pesticidal agricultural applications such as nitrogen fixation.

A policy statement appearing in the June 26, 1986 Federal Register described the comprehensive federal framework for regulating biotechology. This comprehensive framework provides a basic network of agency jurisdiction over both research and commercial products.

As part of the coordinated framework described in the June 1986 Federal Register, EPA is regulating certain products of biotechnology under two laws, TSCA and FIFRA.

TSCA authorizes EPA to acquire information on chemical substances and mixtures of chemical substances to identify and regulate potential hazards and exposures. TSCA's applicability to the regulation of microbial biotechnology products is based on the interpretation that microbes are chemical substances under TSCA. The simplified basis for this interpretation is that all substances, living and non-living, have a chemical foundation at the most fundamental molecular level. As a result of this interpretation, microorganisms are subject to all provisions of TSCA, except for categories of organisms explicitly

excluded under Section 3 of TSCA, i.e., those covered by other statutes such as microorganisms processed or distributed in commerce for use as pesticides, foods, food additives, drugs, cosmetics, or other related items.

FIFRA establishes EPA's authority over the distribution, sale, and use of all pesticide products, including microbial pesticides. FIFRA authorizes EPA to regulate pesticides through a registration process. Microbial pesticides have been registered for almost 20 years, and the Agency was able to draw on this experience in developing its policy for regulating microbial products of biotechnology.

FIFRA specifies that a pesticide can be registered for use only if the pesticide will not cause unreasonable adverse effects to humans or the environment. In order to register a pesticide, an applicant must submit or cite data on subjects such as product composition, human health effects, environmental fate, and effects on nontarget organisms.

I would now like to briefly describe the Agency review process for products of biotechnology that are to be tested or used in the environment.

EPA's reviews under FIFRA and TSCA of submissions involving environmental testing of genetically engineered microorganisms are summarized in Appendices A and B.

The Agency is dedicated to using a comparable review process under TSCA and FIFRA. At this time, reviews are conducted on a case-by-case basis.

When a submission for small-scale field testing is received under FIFRA, EPA staff evaluate the submission and develop a scientific position. During this process, any potential problems, issues, or significant unanswered questions are identified and the likelihood of significant risk from the proposed field testing is addressed.

Similarly, for a submission involving small-scale field testing received under the TSCA provisions, EPA staff groups assess hazard and exposure, and integrate their conclusions in a coordinated risk assessment.

Under both TSCA and FIFRA, intra-Agency workgroups then comment on the positions developed by staff. If appropriate, the submission and EPA's scientific position are sent to other Federal agencies for comment. Appropriate State regulatory agencies are also contacted to alert them to the submission, to discuss EPA's assessments, and to ensure that the Federal and State positions are as consistent as possible.

In some cases, to obtain an independent peer review of the Agency's scientific position, to address specific scientific questions raised by the Agency, or to identify any additional data that may be needed to complete the risk assessment, the submission and the Agency's scientific evaluations are sent to a group of independent scientists constituted as a subcommittee of an Agency advisory group. The Agency has established a specific advisory committee, the Biotechnology Science Advisory Committee (BSAC) for these independent peer reviews. Prior to

the establishment of BSAC, the FIFRA Scientific Advisory Panel (SAP) performed this function for genetically engineered and nonindigenous microbial pesticides. Several proposed field trials have been reviewed by either BSAC or SAP subcommittees and these groups have endorsed EPA assessments.

Public comment is considered an important aspect of reviews, and for many proposals the public is provided several opportunities to comment during the review process.

At the conclusion of a review, the Agency determines whether the microorganism may be released into the environment. Under both TSCA and FIFRA, this decision is based on an assessment of both the potential risks and the potential benefits of the proposed use of the microorganism. Should the analysis indicate that use of the microorganism may pose unreasonable risks, the Agency has authority under either statute to impose restrictions on its use.

I believe that EPA's scientific review process is credible, sound and respected by the scientific community, while assuring that potential human or environmental impacts have been addressed. In addition, I feel confident that EPA's regulatory programs will protect the public health and the environment from unreasonable risks while allowing all of us to reap the benefits of scientific and technological innovations.

That completes my prepared statement, Mr. Chairman. I would be a happy to answer any questions the Subcommittee may have.

APPENDIX A

SUMMARY OF REVIEWS CONDUCTED UNDER TSCA AND FIFRA

This summary describes reviews which have been conducted or are being conducted under the Toxic Substances Control Act (TSCA) and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) through April 27, 1988.

SUMMARY OF PMNs FOR MICROORGANISMS UNDER TSCA

Testing in the Environment

Applicant; Type of Product	Chronology of Events	Major Issues
BioTechnica • rDNA addition products • 2 strains of nitrogen-fixing bacteria to enhance yield of alfalfa • Rhizobium meliloti	• February 1987; submission received • March 1987; BSAC sub-committee meeting • May 1987; preliminary decision to approve test suspension of review to develop consent order • August 1987; Review suspended for additional two months as Company develops monitoring protocols and background monitoring data • October 1987; Additional data data and protocols received from Company • March 1988; review completed. Consent Order issued to ensure proper conduct of proposed field test • April 1988; Company will initiate field test	• Agency has sufficent data to conclude field test is low risk • Monitoring methods and protocols from the company are needed • Consent order ensures test conducted with constraints determined by Agency as necessary and ensures data developed
Monsanto • rDNA addition product • product to monitor microorganism under field conditions • Pseudomonas aureofaciens marked with genes from E. coli	• June 1987; submission received • August 1987; BSAC subcommittee meeting • September 1987;prelimary decision to approve test review suspended to develop consent order • October 1987; review completed • November 2, 1987; test conducted	• Agency has sufficent data to conclude field test is low risk • Although not needed prior to this small-scale field test, information on economic impact on water quality testing and dairy product shelf-life is needed to evaluate widespread releases, company developing this information • Consent order ensures test conducted with constraints determined by Agency as necessary and ensures data developed

SUMMARY OF PMNs FOR MICROORGANISMS UNDER TSCA

Testing in the Environment

Applicant; Type of Product	Chronology of Events	Major Issues
BioTechnica, Agriculture, Inc. (BTA) • rDNA addition products • 8 strains of nitrogen-fixing bacteria to enhance yield of alfalfa • Rhizobium meliloti	• March 1988; submission received	• None identified at this time

SUMMARY OF PMNs FOR MICROORGANISMS UNDER TSCA

Use in Closed Systems

Applicant; Type of Product	Chronology of Events	Major Issues
International Minerals and Chemical Co. • rDNA addition products • E. coli engineered to contain human gene for insulin-like growth hormone • Use as a component in cell culture media	• February 1987; submission received • May 1987; review completed, product judged to be of low risk, no regulatory action taken	• None identified at this time
Company Name Confidential • addition product • Bacillus subtilis engineered for enhanced production of a protease • commercial product (kind and name of product confidential)	• May 1987; submission received • July 1987; review completed, product judged to be of low risk, no regulatory action taken	• None identified at this time
Company Name Confidential • addition product • Bacillus engineered for enhanced production of hydrolase • commercial product (kind and name of product confidential)	• July 1987; submission received • October 1987; review completed, product judged to be of low risk, no regulatory action taken	• None identified at this time
Company Name Confidential • self-cloned to contain multiple copies using plasmid vector from Staphylococcus aureus • Bacillus alcalophilus engineered for enhanced production of protease • commercial product (kind and name of product confidential)	• April 1988, submission received	• None identified at this time

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Advanced Genetic Sciences (AGS) Notification		
• rDNA deletion product • INA^- bacteria for frost protection • Pseudomonas syringae and Pseudomonas fluorescens	• November 1984; Notification received • January 1985; SAP subpanel meets • February 1985; Letter to AGS requesting additional information and an EUP	• Potential adverse effect on plants, insects, weather patterns • Competitiveness of INA^- products and potential to displace INA^+ bacteria
Mycogen (informal review)		
• rDNA addition product • B. thuringiensis toxin gene inserted into Pseudomonas for insect control; CELLS KILLED	• April 1985; Notification received • June 1985; Mycogen informed that Interim Policy does not apply to their killed product	• Applicability of Interim Policy • Mycogen provided data to substantiate non-viability of their product
United States Dept. of Agriculture (USDA) Notification		
• Undirected mutagenesis product Two species of fungi to be used to control pest fungi • Trichoderma viride and T. harzianum	• January 1985; Notification received • April 1985; 90 day clock suspended; EPA requests additional information • May 1985; USDA withdraws notification	• Relative level of risk produced by products of undirected mutagenesis compared to other altered products • The extent of data and information needed (and practical to obtain) on these products for a notification

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Advanced Genetic Sciences (AGS) EUP • rDNA deletion product • INA⁻ bacteria for frost protection of plants • Pseudomonas syringae and P. fluorescens	• July 1985; EUP application received • August 1985; receipt announced in Federal Register • September 1985; public comment received • September/October 1985; SAP and intra-Agency review of comments • November 1985; approval announced • November 1985; Agency sued by Foundation on Economic Trends • February 1986; outdoor testing of rDNA deletion product disclosed • March 1986; EPA audits AGS and suspends EUPs • June 1986; civil complaint issued against AGS for violation of EUP regulations, penalty $20,000 • July 1986; consent agreement and final order signed, settlement $13,000 • July 1986; EPA reviews and approves AGS plant pathogenicity retest • December 1986; AGS submits information on proposed test sites • February 1987; EPA approves test sites, reinstates EUPs • March 1987; AGS selects Brentwood site in Contra Costa County to run test • April 1987; AGS sued, injunction requested, request overruled, strawberry plot vandalized • April 24, 1987; AGS test INA⁻ bacteria, EPA monitors for aerial dispersion • August 1987; AGS submits summary of results of field trial	• AGS submitted documentation of findings as requested • Additional data submitted on competitiveness, plant pathogenicity, and colonization, identification and detection • Assertions of low risk substantiated by data • Some plant pathogencity data called into question due to methods used • EPA reinstatement of EUPs pending test site • Evaluation of monitoring results to determine whether minimal risk conclusions (based on lab and greenhouse data) were borne out by observation in field

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

AGS
Amendment to EUP

• September 1987; AGS requests EUP amendment to conduct 2nd test at same site	Field trial slightly expanded in acreage # of plants, # of application 2 spray applications (November/March) Reduction in protective clothing proposed
• November 1987; EPA amends EUP	
• December 1987; AGS initiated 2nd small-scale field test; monitoring of treated plants to continue through Spring 1988. To date, monitoring indicates minimal off-site dispersal and colonization.	

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Monsanto Notification		
• rDNA addition product • B. thuringiensis toxin gene inserted into Pseudomonas fluorescens for insect control	• January 1985; Notification received • March 1985; SAP subpanel meeting • April 1985; letter to Monsanto requesting additional information and an EUP	• Could toxin gene insertion mechanism cause environmental problem • Possible adverse effects on non-target species
Monsanto EUP		
• rDNA addition product • B.t. toxin gene inserted into P. fluorescens for insect control	• October 1985; EUP application received • April 1986; SAP subpanel and other agency review EPA inspection of proposed test site • May 1986; EPA conducts books and records check, informs Monsanto additional data needed • September 1986; EPA reviews test protocols submitted by Monsanto for use in development of additional data • November 1987; EUP review suspended pending receipt of additional data	• Agency reviews data generated by company to address major scientific issues identified in Notification • Determination of Confidential Business Information status of submission • Questions of colonization and effects on non-targets not fully addressed by available data
Sands Notification		
• Undirected mutagenesis (UV) product • Derived strains of Sclerotinia sclerotiorum to be used to control plant pests	• May 1986; Notification received • July 1986; SAP and other agencies review • August 1986; EPA announces decision - no EUP required	• Relative risk compared to parental strain which is wide host range plant pathogen • Contingency plans for test termination

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Harman Notification		
• Protoplast fusion product • Hybrid strains of *Trichoderma harzianum* to be used to control pest fungi	• June 1986; Notification received • July 1986; SAP and other agencies review • September 1986; EPA informs Harman no EUP necessary	• Relative risk compared to parental strains • Competitiveness and effects on beneficial fungi • Extent of data and information needed for this type of product
Ecogen (I) Notification		
• Plasmid cured and transconjugant strains of *Bacillus thuringiensis* varieties *kurstaki* and *azawai* to be used to control lepidopteran pests	• May 1986; Notification received • July 1986; SAP and other agencies review • June 1986; EPA announces decision - no EUP required	• Applicability of Interim Policy to these products • Relevance of existing data base on *B. thuringiensis* • Probability that plasmid cured and transconjugant strains occur naturally
Ecogen (II) Notification		
• Plasmid cured and transconjugant strains of *B. thuringiensis* • Test on potatoes • Includes new strain active against beetles	• March 4, 1987; Notification received • April 17, 1987; EPA informs Ecogen no EUP necessary	• Expedited review • Risk issues similar to submission (I) • Additional host range risk issue due to new toxin active against beetles
Ecogen (III) Notification		
• *B. thuringiensis* strains similar to submission (I) • Test on cotton and vegetables	• March 20, 1987; Notification received • May 12, 1987; Ecogen informed no EUP is necessary	• Expedited review • Risk issues similar to submission (I)

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Ecogen (IV) Notification		
• *B. thuringiensis* strains similar to submission (I) • Test on forest trees	• April 10, 1987; Notification received • April 27, 1987; EPA informs Ecogen no EUP necessary	• Expedited review • Risk issues similar to submission (I) • Additional risk issue due to forest use and exposure to forest non-target organisms • Uses strains active against Lepidoptera and Coleodoptera
University of Arkansas Notification		
• Herbicidal fungus • Chemically induced mutant (benomyl-resistant) of *Colletotrichum gloeosporiodes*, an EPA registered product (Collego) • Use on rice and soybeans to control joint vetch	• April 1987; Notification received • June 1987; Comments received from USDA/APHIS • July 1987; EPA informs university no EUP necessary	• Expedited review • Minor genetic modification using classical chemical-induced mutagenesis, no new genetic information added • Possible host range changes (microbial herbicides are plant pathogens)
University of California Notification		
• rDNA deletion product • *Pseudomonas syringae* to be used for frost protection for plants	• December 1984; Notification received • February 1985; SAP provided comments • March 1985; letter requesting additional data and an EUP • June 1985; OPP met with NIH and Cabinet Council to discuss the two Agency's reviews and conclusions concerning INA-bacteria.	• Potential adverse effects on plants, weather patterns • Competitiveness of INA^- products to displace INA^+ bacteria

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
University of California EUP		
• rDNA deletion product • INA⁻ bacteria for frost protection of plants	• December 1985; EUP application received • May 1986; EPA inspects test site, participates in public meeting, conducts books and records check • June 1986; EPA grants EUP • July 1986; EPA conducts "mock" application with aerial monitoring • August 1986; University of California and CDFA sued by the Foundation on Economic Trends et. al. experiment postponed pending development of further information • April 1987; University issued go ahead for experiment • April 1987; INA⁻ treated potato seed pieces planted • May 28, 1987; plot vandalized spray application of INA⁻ EPA conducts aerial monitoring • August 1987; INA- treated potato seed pieces planted for second time • January 1988; monitoring indicates minimal off-site dispersal & colonization. Lindow submitted EUP amendent to modify monitoring program; under review by EPA.	• Agency reviews data generated by applicant to address major scientific issues identified in Notification

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
McNeese Notification		
• nonindigenous protozoa (from Thailand) to control mosquitos • Amblospora aedes	• May 1985; Notification received • July 1985; EPA informs applicant that additional data needed to support notification • August 1985; Notification resubmitted with more information • September 1985; EPA meets with USDA to discuss adequacy of data • October 1985; EPA informs McNeese submitted data inadequate; McNeese also asked to comply with applicable USDA/APHIS requirements • November 1987; EPA review suspended pending receipt of additional information	• The amount of data and information needed (and practical to obtain) to adequately assess risks and determine need for an EUP
Montana State Notification		
• Transposan mediated mutagenesis of Pseudomonas syringae to control Dutch Elm disease	• June 22, 1987; received notification • July 31, 1987; HED interim risk assessment completed • August 27, 1987; a letter of reprimand forwarded from Moore to Montana State President	• Dr. Strobel initiated testing before getting approval

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Harmon Notification		
• Protoplast fusion products of *Tridrodema harzianum*	• January 1988; notification received; expansion of testing conducted in 1987 • April 1988; Harmon informed that EUP is not required	• None identified at this time
Ecogen (V) Notification		
• *Bacillus thuringiensis* strain similar to Ecogen (I) • Test on cotton and vegetables	• July 10, 1987; received notification • Risk assessment completed • September 1987; Ecogen informed that EUP is not required	• Uses strains active Lipidopera and Coleoptera • Risk issues similar to Ecogen (I)
Ecogen (VI) Notification		
• Similar to Ecogen (I)	• July 10, 1987; received notification • A generic risk assessment of *B. thuringiensis* products derived by conjugation and/or plasmid curing initiated by HED • September 1987; Ecogen informed that EUP is not required	• Will grant an exemption from the requirement for notification to Ecogen *B. thuringiensis* strains derived by plasmid curing and transconjugation • Includes a description of areas of endangered species to be avoided
Ecogen (VII) 4 EUPs		
• Various *B. thuringiensis* transconjugants for several uses.	• January/February, 1988; application received. under review.	

SUMMARY OF NOTIFICATIONS AND EXPERIMENTAL USE PERMITS FOR MICROORGANISMS UNDER FIFRA

Applicant; Type of Submission and Type of Product	Chronology of Events	Major Issues
Crop Genetics EUP		
• Clavibacter xyli, a bacterium that lives in plants, it has a B. thuringiensis toxic gene inserted to control corn borers	• December 28, 1987; application received • March 1988; public comment received, preliminary risk assessment completed, provided to BSAC & available to public upon request • April 1988; BSAC subcommittee meeting scheduled for April 18, decision expected in early May	
Sandoz Notification		
• Transconjugant B. thuringiensis strains • Microbial insecticide	• March 1988; notification received; under review	

APPENDIX B

INFORMATION SPECIFICALLY REQUESTED BY THE SUBCOMMITTEE

QUESTION #1

Since October 1, 1986, the number of applications received by EPA for review of planned introductions of genetically engineered organisms into the environment.

Under Toxic Substances Control Act (TSCA)

EPA has received a total of 16 premanufacture notifications (PMNs) for biotechnology products. Twelve of these PMNs were applications for the testing of genetically engineered microorganisms in the environment and four for closed system uses.

Under Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)

EPA has received 12 applications under FIFRA for review for release of genetically engineered microorganisms into the environment.

QUESTION #2

A general description of the types of organisms for which applications have been received since October 1, 1986.

Under TSCA - Environmental Releases

EPA received 3 PMNs for environmental testing of a nitrogen-fixing bacterium (Rhizobium meliloti) genetically engineered for yield enhancement in alfalfa. The PMNs were submitted in February 1987, approved in March 1988 and field testing initiated in April 1988.

EPA received a PMN for environmental testing of a common soil bacterium (Pseudomonas fluorescens) engineered to contain genes from Escherichia coli. The added genes provide a "marker" system to enhance the capability for monitoring the microorganism under field conditions. The PMN was submitted in June 1987, approved in October 1987 and field testing initiated in November 1987.

EPA is currently reviewing eight PMNs for environmental testing of a nitrogen-fixing bacterium (Rhizobium meliloti) genetically engineered to enhance yield in alfalfa and to facilitate environmental monitoring through the use of antibiotic resistance markers. The PMN was submitted in March 1988.

Under TSCA - Closed-System Uses

EPA received a PMN for a strain of Escherichia coli engineered to contain a human gene for insulin-like growth hormone. The growth hormone will be used as a component of cell culture media. The PMN was submitted in February 1987 and the review completed in May 1987. No regulatory action was taken because the product was judged to be low risk.

EPA received a PMN for a strain of Bacillus subtilis engineered for enhanced production of an enzyme, protease. The protease will be used in a commercial product. The PMN was submitted in May 1987 and the review completed in July 1987. No regulatory action was taken because the product was judged to be low risk.

EPA received a PMN for a strain of Bacillus engineered for enhanced production of an enzyme, hydrolase. The hydrolase will be used in a commercial product. The PMN was submitted in July 1987 and the review completed in October 1987. No regulatory action was taken because the product was judged to be low risk.

EPA received a PMN for a strain of Bacillus alcalophilus, modified to contain multiple copies of a gene coding for a protease enzyme; plasmid vectors from Staphyloccus aureus were used in the engineering. The PMN was submitted in April 1988 and is currently under review.

Under FIFRA

A general description of the types of organisms for which applications have been received under FIFRA since October 1, 1986 are listed in Appendix A.

QUESTION #3

The number of applications received since October 1, 1986, which have been reviewed by a scientific advisory panel.

Under TSCA

The four PMN submissions which involved environmental release were reviewed by a subcommittee of the Agency's Biotechnology Science Advisory Committee.

Under FIFRA

Prior to the formation of the Agency's Biotechnology Science Advisory Committee, submissions under FIFRA were reviewed by a subpanel of the FIFRA Scientific Advisory Panel (SAP). Since October 1, 1986, two submissions have been reviewed by mail by a

SAP subpanel; one has been reviewed by the subpanel Chairman for a determination of whether a full subpanel review was necessary; and six modifications have been reviewed by the Agency in light of a subpanel review of the original submission prior to October 1, 1986. In addition, one submission has been reviewed at a meeting of a subcommittee of the Agency's Biotechnology Science Advisory Committee.

QUESTION #4

The number of applications received since October 1, 1986, which have been approved.

Under TSCA

To date, EPA has reviewed four PMNs involving environmental release and has allowed them to proceed with restrictions. These include:

- three constructs of a nitrogen-fixing bacterium (Rhizobium meliloti) genetically engineered for yield enhancement in alfalfa; and
- a strain of common soil bacterium (Pseudomonas fluorescens) engineered to contain genes from Escherichia coli.

To date, EPA has also reviewed three PMNs for closed system use and has allowed them to proceed without restrictions. These include:

- a strain of Escherichia coli engineered to contain a human gene for insulin-like growth hormone;
- a strain of Bacillus subtilis engineered for enhanced production of a protease, an enzyme; and
- a strain of Bacillus engineered for enhanced production of a hydrolase, an enzyme.

Under FIFRA

Nine applications have been approved. One application was withdrawn and two are under review.

QUESTION #5

The number of applications received since October 1, 1986, which have been denied.

Under TSCA

None

Under FIFRA

None

QUESTION #6

The number of applications received since October 1, 1986, which required a request for additional information.

Under TSCA

EPA's review of all four PMNs involving environmental testing required the companies to submit additional information and/or data. In the case of the three PMNs on nitrogen-fixing bacteria, monitoring protocols were required. For the PMN on a common soil bacterium, water quality test data were required.

EPA's review of the Bacillus strain engineered for enhanced production of hydrolase was suspended for two weeks pending receipt of further information requested by EPA. EPA believed that this information was needed before it could complete its review of the product.

Under FIFRA

Six applications have required further information before the review could be completed.

QUESTION #7

The number of applications received since October 1, 1986, which were reviewed by EPA and at least one other federal agency.

Under TSCA

Reviews of all four PMNs involving environmental testing were coordinated with USDA. All four PMNs were allowed to proceed subject to conditions specified by EPA and agreed to by the companies in what is termed a "consent order" issued under section 5(e) of TSCA.

Two applications for closed-system use (Escherichia coli and Bacillus engineered for production of hydrolase) were reviewed by both EPA and FDA.

EPA is now reviewing a product for a closed-system use. (*Bacillus alcalophilus* engineered to enhance production of a protease enzyme. This product is also being reviewed by the Consumer Product Safety Commission (CPSC)).

Under FIFRA

Eleven applications were reviewed by EPA and at least one other federal agency.

Mr. SCHEUER. Dr. Gilles?

Dr. GILLES. Thank you, Mr. Chairman.

USDA, along with other agencies, has stated the policy that basically we believe that the existing statutes are adequate for regulating the products of biotechnology, that such products would not differ fundamentally from those produced by conventional methods and that the products and the risks should be regulated rather than the technology. We believe this posture, that we have assumed for several years, is consistent with the report of the National Academy of Science to which you referred earlier and largely to the Office of Technology report, which we've had an opportunity to briefly look at just today. Certainly on pages 4, 87 and 88, these concepts are carried.

Within the USDA, the regulatory responsibilities fall under the Assistant Secretary for Marketing and Inspection, the research responsibilities under the Assistant Secretary for Science and Education. A coordinating body called the Committee for Biotechnology in Agriculture, which comprises the six agency administrators which are responsible for biotechnology, meets periodically to establish policy and to coordinate our resources.

Basically, we have the resources through the various laws to permit us to regulate veterinary biologics, the plant pests, and to this end we have received to date something of the order of 48 applications in the period of October of '86 through April of '89, of which 23 were for plants and microorganisms and 25 were for veterinary biologics.

The types of organisms vary to a considerable extent, and these are articulated in the report.

To meet our needs in research and in education, the Department has established a series of external communications. We had a challenge forum last year, and we have had four discussions this year in which the biotechnology for agriculture has been presented at several different locations, and next week there will be a public presentation in Minneapolis. I believe a copy of that program has been appended to these minutes. And the participation has been very good. Also the presenters are members not only of the USDA, but of the other regulatory agencies as well as the private sector.

I believe that we are endeavoring to meet the responsibilities as we see them, and certainly one of the major challenges that was pointed out in your opening remarks is to use the best science possible to facilitate the increasing competitiveness that we do face in the international sphere as far as biotechnology applications are concerned.

Thank you, Mr. Chairman. These are very brief, abstracted comments.

[The prepared statement of Dr. Kenneth Gilles follows:]

STATEMENT OF DR. KENNETH A. GILLES
ASSISTANT SECRETARY, MARKETING AND INSPECTION SERVICES
U.S. DEPARTMENT OF AGRICULTURE
BEFORE THE
HOUSE COMMITTEE ON SCIENCE, SPACE AND TECHNOLOGY
SUBCOMMITTEE ON NATURAL RESOURCES
AGRICULTURE, RESEARCH AND ENVIRONMENT

MAY 5, 1988

MR. CHAIRMAN AND MEMBERS OF THE SUBCOMMITTEE, IT IS A PLEASUPE TO APPEAR BEFORE YOU TODAY TO DISCUSS THE DEPARTMENT OF AGRICULTURE'S (USDA) EXPERIENCE IN THE REGULATION OF BIOTECHNOLOGY AND THE IMPLICATIONS OF THE OFFICE OF TECHNOLOGY ASSESSMENT'S (OTA) REPORT FOR REGULATION AND RESEARCH. BECAUSE WE HAVE HAD LIMITED TIME TO REVIEW IN DETAIL THE OTA REPORT, WE ARE NOT ABLE TO DISCUSS IT AT LENGTH IN OUR TESTIMONY, BUT WE WILL ENDEAVOR TO RESPOND TO ANY QUESTIONS YOU MAY HAVE.

BIOTECHNOLOGY OFFERS GREAT POTENTIAL IN MANY AREAS, PARTICULARLY IN CONTINUING IMPROVEMENT OF OUR CAPACITY TO DEVELOP PRODUCTS THAT ARE OF CRITICAL IMPORTANCE TO THE FUTURE OF AMERICAN AGRICULTURE. IT IS VITAL THAT PRODUCTS OF BIOTECHNOLOGY BE REGULATED BASED ON FIRM SCIENTIFIC PRINCIPLES AND MEET THE SAME HIGH STANDARDS OF SAFETY AND EFFICACY AS DO THOSE PRODUCTS MADE THROUGH CONVENTIONAL TECHNOLOGY. THUS, WE SEEK TO FOSTER A REGULATORY CLIMATE THAT ENCOURAGES INNOVATION, DEVELOPMENT, AND COMMERCIALIZATION OF BENEFICIAL NEW AGRICULTURAL PRODUCTS DERIVED FROM BIOTECHNOLOGY, WHILE IMPLEMENTING A RESPONSIBLE POLICY THAT LIMITS POTENTIAL OF REAL RISKS.

USDA, ALONG WITH OTHER FEDERAL AGENCIES, STATED ITS POLICY FOR REGULATING BIOTECHNOLOGY IN DECEMBER 1984, AND JUNE 1986, AS PART OF THE "COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY." THE USDA POLICY IS BASED ON THREE MAIN ELEMENTS:

-- THE EXISTING STATUTES ARE ADEQUATE FOR REGULATING THE PRODUCTS OF AGRICULTURAL BIOTECHNOLOGY;

-- USDA DOES NOT ANTICIPATE THAT SUCH PRODUCTS WOULD DIFFER FUNDAMENTALLY FROM THOSE PRODUCED BY CONVENTIONAL METHODS;

-- THE PRODUCT AND THE RISK SHOULD BE REGULATED, RATHER THAN THE TECHNOLOGY.

THESE ELEMENTS ARE CONSISTENT WITH THE NATIONAL ACADEMY OF SCIENCES REPORT THAT WAS ISSUED 1987.

ORGANIZATION

THE USDA CARRIES OUT ITS REGULATORY RESPONSIBILITY UNDER THE GENERAL SUPERVISION OF THE ASSISTANT SECRETARY FOR MARKETING AND INSPECTION SERVICES; ITS RESEARCH RESPONSIBILITIES UNDER THE ASSISTANT SECRETARY FOR SCIENCE AND EDUCATION. TO COORDINATE RESOURCES, ADMINISTRATORS OF THE SIX AGENCIES PRIMARILY RESPONSIBLE FOR BIOTECHNOLOGY PROGRAMS TOGETHER WITH THE TWO ASSISTANT SECRETARIES COMPRISE THE COMMITTEE FOR BIOTECHNOLOGY IN AGRICULTURE (CBA). THE CBA MEETS TO DISCUSS AND RESOLVE SCIENTIFIC AND POLICY ISSUES. IT REPORTS TO THE SECRETARY OF AGRICULTURE ON INTERNAL MATTERS, AND TO THE BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE (BSCC) ON MATTERS OF OVERALL

FEDERAL POLICY FOR BIOTECHNOLOGY.

SUPPORT STAFF FOR THE CBA IS REPRESENTED IN THE OFFICE OF AGRICULTURAL BIOTECHNOLOGY, THE DIRECTOR OF WHICH REPORTS TO THE DEPUTY SECRETARY. WITHIN APHIS, WE HAVE ESTABLISHED THE BIOTECHNOLOGY AND ENVIRONMENTAL COORDINATION (BEC) STAFF TO COORDINATE THE DEPARTMENT'S REGULATORY ACTIVITIES. THE BEC STAFF ALSO TAKES THE LEAD IN LIAISON BETWEEN APHIS AND OTHER FEDERAL AGENCIES ON BIOTECHNOLOGY REGULATORY MATTERS.

REGULATION

STATUTES ADMINISTERED BY USDA AND APPLICABLE TO THE REGULATION OF BIOTECHNOLOGY WERE LISTED IN THE FINAL USDA POLICY STATEMENT, WHICH WAS PUBLISHED IN THE FEDERAL REGISTER ON JUNE 26, 1986. THE USDA REGULATORY AGENCIES ADMINISTERING THESE STATUTES ARE THE ANIMAL AND PLANT HEALTH INSPECTION SERVICE (APHIS), THE FOOD SAFETY AND INSPECTION SERVICE, AND THE AGRICULTURAL MARKETING SERVICE. BECAUSE APHIS HAS BEEN ACTIVELY INVOLVED IN REGULATING THE TESTING AND DEVELOPMENT OF GENETICALLY ENGINEERED ORGANISMS, I WILL FOCUS MY COMMENTS ON THE APHIS EFFORT.

THROUGH A VARIETY OF STATUTES, APHIS HAS AUTHORITY TO REGULATE ORGANISMS AND VECTORS WHICH MAY SPREAD OR CAUSE DISEASES OF LIVESTOCK OR POULTRY; VETERINARY BIOLOGICAL PRODUCTS; AND PLANTS, PLANT PRODUCTS OR PLANT PESTS WHICH MAY CAUSE INJURY, DISEASE, OR DAMAGE TO PLANTS.

VETERINARY BIOLOGICS

ORGANISMS AND VECTORS WHICH ARE OR MAY CONTAIN ANIMAL PATHOGENS ARE REGULATED

UNDER THE ACT OF FEBRUARY 2, 1903, AND THE VIRUS SERUM TOXIN ACT OF 1913 (THE VSTA). THE VSTA, WHICH GIVES USDA AUTHORITY OVER VETERINARY BIOLOGICS THAT ARE SHIPPED INTERSTATE OR IMPORTED, WAS AMENDED IN 1985 TO EXTEND AUTHORITY TO PRODUCTS THAT ARE SHIPPED INTRASTATE OR EXPORTED. THE 1985 AMENDMENTS ALSO GAVE USDA ADDITIONAL ENFORCEMENT MECHANISMS. APHIS PUBLISHED FINAL REGULATIONS IMPLEMENTING THESE AMENDMENTS DURING THE SPRING AND SUMMER OF 1987. THESE REGULATIONS STRENGTHEN AND EXTEND USDA'S AUTHORITY AT A CRITICAL TIME IN THE DEVELOPMENT OF VETERINARY BIOLOGICS PRODUCED BY RECOMBINANT DNA TECHNOLOGY.

APHIS ISSUES U.S. VETERINARY BIOLOGICAL PRODUCT LICENSES AFTER A MANUFACTURER SATISFACTORILY COMPLETES ALL REQUIREMENTS, WHICH ARE DESIGNED TO ENSURE THAT THE PRODUCT IS PURE, SAFE, POTENT, AND EFFICACIOUS. VETERINARY BIOLOGICAL PRODUCTS PRODUCED BY RECOMBINANT METHODS ARE EVALUATED ON A CASE-BY-CASE BASIS USING THE SAME STRINGENT STANDARDS FOR LICENSING EMPLOYED FOR CONVENTIONALLY PRODUCED BIOLOGICS.

FOR VETERINARY BIOLOGICAL PRODUCTS THAT ARE RECOMBINANT-DERIVED OR DERIVED FROM MONOCLONAL ANTIBODIES, A THREE-CATEGORY CLASSIFICATION SYSTEM BASED ON BIOLOGICAL CHARACTERISTICS AND SAFETY CONCERNS WAS PUBLISHED IN THE FEDERAL REGISTER AS A PART OF THE USDA POLICY STATEMENT ON BIOTECHNOLOGY IN JUNE 1986.

CATEGORY ONE PRODUCTS INCLUDE INACTIVATED OR KILLED RECOMBINANT DNA-DERIVED VACCINES, BACTERINS, AND MONOCLONAL ANTIBODY (HYBRIDOMA) PRODUCTS USED THERAPEUTICALLY OR AS COMPONENTS IN DIAGNOSTIC TEST KITS. SEVENTEEN LICENSES HAVE BEEN ISSUED FOR CATEGORY ONE PRODUCTS SINCE OCTOBER 1, 1986.

CATEGORY TWO PRODUCTS INCLUDE THOSE PRODUCTS CONTAINING LIVE MICROORGANISMS THAT HAVE BEEN MODIFIED BY THE ADDITION OR DELETION OF ONE OR MORE GENES. TWO LICENSES FOR CATEGORY TWO PRODUCTS HAVE BEEN ISSUED FOR RECOMBINANT-DERIVED MODIFIED LIVE VIRUS PSEUDORABIES VACCINES DURING THE LAST TWENTY MONTHS. BEFORE GRANTING THESE LICENSES, APHIS GRANTED AUTHORIZATION FOR FIELD TRIALS IN SUPPORT OF THE LICENSE APPLICATIONS. APHIS PREPARED EXTENSIVE ENVIRONMENTAL ASSESSMENTS OF THE IMPACTS OF ALLOWING THE FIELD TRIALS AND THE IMPACTS OF GRANTING PRODUCT LICENSES FOR THESE CATEGORY TWO PRODUCTS. IN EACH CASE, THE ENVIRONMENTAL ASSESSMENT RESULTED IN A FINDING OF NO SIGNIFICANT IMPACT.

CATEGORY THREE PRODUCTS ARE THOSE PRODUCTS WHICH INCLUDE PRODUCTS USING LIVE VECTORS TO CARRY RECOMBINANT-DERIVED FOREIGN GENES THAT CODE FOR IMMUNIZING ANTIGENS OR OTHER IMMUNE STIMULANTS. TO DATE, APHIS HAS NOT ISSUED ANY LICENSES FOR CATEGORY THREE PRODUCTS. HOWEVER, USDA HAS BEEN CONTACTED BY A COMMERCIAL AND A RESEARCH INSTITUTE CONCERNING DATA THAT WOULD BE NEEDED IN AN ENVIRONMENTAL ASSESSMENT FOR THE RELEASE OF A LIVE VECTORED BIOLOGICAL PRODUCT.

PLANT PESTS

THE AGENCY HAS USED ITS EXISTING STATUTORY AUTHORITY UNDER THE FEDERAL PLANT PEST ACT AND THE PLANT QUARANTINE ACT TO ISSUE A NEW RULE FOR GENETICALLY ENGINEERED ORGANISMS OR PRODUCTS WHICH ARE OR MAY BE PLANT PESTS. THE FINAL RULE, WHICH TOOK EFFECT ON JULY 16, 1987, ESTABLISHED PERMIT AND OTHER REQUIREMENTS FOR THE IMPORTATION, INTERSTATE MOVEMENT, AND RELEASE INTO THE ENVIRONMENT OF GENETICALLY ENGINEERED ORGANISMS AND PRODUCTS THAT ARE OR MAY BE PLANT PESTS. A PRODUCT IS REGULATED FOR ITS POTENTIAL RISK IF THE PRODUCT

CONSISTS OF OR CONTAINS AN ORGANISM LISTED AS A PLANT PEST IN THE FINAL RULE. THE RULE ALSO GIVES APHIS AUTHORITY TO REGULATE ANY OTHER ORGANISM OR PRODUCT PRODUCED THROUGH GENETIC ENGINEERING WHEN THE AGENCY DETERMINES THAT IT IS A PLANT PEST OR WHEN WE HAVE REASON TO BELIEVE IT IS A PLANT PEST. THE RULE REQUIRES THAT WE NOTIFY AFFECTED STATES SO THAT THEY MAY REVIEW PERMIT APPLICATIONS. WE ALSO PUBLISH NOTICES DESCRIBING GENETICALLY ENGINEERED ORGANISMS FOR WHICH WE HAVE RECEIVED PERMIT APPLICATIONS AND WHICH ARE BEING REVIEWED FOR ENVIRONMENTAL RELEASE. ALTHOUGH THE RULE WAS PUBLISHED AS A FINAL RULE, IT IS FLEXIBLE AND CAN BE AMENDED. THE RULE ALSO CONTAINS A PROVISION ALLOWING FOR PETITIONS TO AMEND THE LIST OF PLANT PEST ORGANISMS. WE HAVE RECENTLY AMENDED THE RULE TO REMOVE SOME RESTRICTIONS PERTAINING TO THE INTERSTATE MOVEMENT OF CERTAIN MICROORGANISMS UNDER SPECIFIED CONDITIONS THAT WOULD PROVIDE ADEQUATE SAFEGUARDS TO PREVENT THE INTRODUCTION AND DISSEMINATION OF PLANT PESTS.

SINCE THE JULY 1987 RULE TOOK EFFECT, APHIS HAS RECEIVED 23 APPLICATIONS FOR ENVIRONMENTAL RELEASE OF GENETICALLY ENGINEERED PLANTS AND MICROORGANISMS AND WE HAVE ISSUED 11 PERMITS FOR RELEASE. FOR EACH APPLICATION FOR RELEASE INTO THE ENVIRONMENT OF AN ORGANISM DEEMED TO BE A REGULATED ARTICLE, APHIS PREPARES A THOROUGH ENVIRONMENTAL ASSESSMENT ACCORDING TO THE REQUIREMENTS OF THE NATIONAL ENVIRONMENTAL POLICY ACT. THUS FAR, FOR EACH FIELD TEST THAT HAS BEEN APPROVED BY APHIS, THE AGENCY HAS DETERMINED THAT THESE TESTS DO NOT PRESENT A RISK OF PLANT PEST INTRODUCTION OR DISSEMINATION. THE ENVIRONMENTAL ASSESSMENTS HAVE CONCLUDED WITH FINDINGS OF NO SIGNIFICANT IMPACT.

OUR REGULATORY ACTIONS HAVE MADE IT POSSIBLE FOR PRODUCTS OF BIOTECHNOLOGY TO MOVE FROM THE LABORATORY TO THE FIELD WHILE RETAINING SAFETY MEASURES AND ENSURING CONTINUED PUBLIC CONFIDENCE IN THE PRODUCTS. ONE OF THE MOST

POSITIVE DEVELOPMENTS IN THE IMPLEMENTATION OF FEDERAL BIOTECHNOLOGY POLICY HAS BEEN THE COORDINATION WITH OTHER FEDERAL AGENCIES THROUGH THE BSCC. USDA SHARES JURISDICTION WITH THE ENVIRONMENTAL PROTECTION AGENCY (EPA) AND THE FOOD AND DRUG ADMINISTRATION (FDA) IN CERTAIN AREAS. COORDINATION AND CONSULTATION HAVE BEEN DEMONSTRATED THROUGH JOINT REVIEWS OF APPLICATIONS BETWEEN EPA AND APHIS, THROUGH COMMITTEE ACTIVITIES, AND THROUGH INDIVIDUAL CONTACTS AMONG SCIENTISTS AND JOINT REPORTS TO THE ORGANIZATION FOR ECONOMIC COOPERATION AND DEVELOPMENT. APHIS HAS CONDUCTED THREE COORDINATED REVIEWS WITH EPA FOR ORGANISMS DETERMINED NOT TO BE PLANT PESTS. APHIS HAS RECEIVED APPLICATIONS FOR PLANTS WHICH HAVE BEEN ENGINEERED TO PRODUCE A PRODUCT THAT EPA DEFINES AS PESTICIDAL. THESE APPLICATIONS WERE SENT TO EPA FOR REVIEW OR COMMENT. ADDITIONALLY A GENETICALLY ENGINEERED MICROBIAL PESTICIDE IS CURRENTLY UNDER REVIEW. THIS REVIEW HAS BEEN FULLY COORDINATED BETWEEN APHIS AND EPA WITH THE APPLICANT BEING ASKED TO SUBMIT A SINGLE SET OF DATA REQUIRED FOR USE BY BOTH AGENCIES.

RESEARCH

USDA ALSO RECOGNIZES THE IMPORTANCE OF MAINTAINING THE PUBLIC'S CONFIDENCE IN THE BIOSAFETY OF AGRICULTURAL RESEARCH. USDA HAS ESTABLISHED THE AGRICULTURAL BIOTECHNOLOGY RESEARCH ADVISORY COMMITTEE (ABRAC) TO REVIEW THE BIOSAFETY ASPECTS OF USDA-FUNDED RESEARCH PROJECTS ON GENETICALLY ENGINEERED ORGANISMS BEFORE THE PROJECTS MOVE FROM THE LABORATORY TO THE FIELD. COMPRISED OF NATIONAL EXPERTS IN SCIENCE, LAW, BIOETHICS, AND ENVIRONMENTAL POLICY, ABRAC'S RECOMMENDATIONS WILL ASSIST SENIOR AGENCY OFFICIALS IN MAKING SCIENCE-BASED DECISIONS ON THE SAFETY OF AGRICULTURAL RESEARCH INVOLVING BIOTECHNOLOGY.

INITIATIVES CONCERNING RESEARCH WILL BE IMPLEMENTED WITH CLOSE COORDINATION

BETWEEN USDA'S REGULATORY AND RESEARCH AGENCIES. A SYSTEM HAS BEEN DESIGNED TO ENSURE A THOROUGH YET TIMELY METHOD FOR INTERAGENCY REVIEWS AND RECOMMENDATIONS.

EDUCATION

THE DEPARTMENT HAS DEVELOPED INTERNAL METHODS OF COORDINATING REGULATIONS AND GUIDELINES, WHICH WILL BE FACILITATED THROUGH THE COOPERATION OF THE RESEARCH COMMUNITY, INDUSTRY, ACADEMIA, AND THE PUBLIC. TO BETTER SERVE THESE IMPORTANT PUBLICS, USDA EMBARKED ON A NATIONWIDE INFORMATION AWARENESS CAMPAIGN IN FEBRUARY 1987.

"BIOTECHNOLOGY: THE CHALLENGE," HELD IN FEBRUARY 1987, WAS THE FIRST OF FIVE CONFERENCES THAT LAID OUT THE IMPORTANT ISSUES FACING TODAY'S BIOTECHNOLOGY COMMUNITIES. THIS FORUM WAS FOLLOWED BY THREE REGIONAL CONFERENCES IN RALEIGH, NORTH CAROLINA, RENO, NEVADA, NEW BRUNSWICK, NEW JERSEY, AND A FOURTH TO BE HELD IN MINNEAPOLIS, MINNESOTA IN MAY 1988.

SPONSORED BY USDA, AMERICA'S LAND GRANT UNIVERSITIES, STATE AGRICULTURAL EXPERIMENT STATIONS, AND THE COOPERATIVE EXTENSION SERVICE, THE FOUR REGIONAL CONFERENCES, CALLED "AGRICULTURAL BIOTECHNOLOGY AND THE PUBLIC" WERE DESIGNED TO DISCUSS PUBLICLY THE LATEST DEVELOPMENTS IN AGRICULTURAL BIOTECHNOLOGY AND INFORM THE CITIZENRY. IN A MILIEU OF OPENNESS AND HELPFULNESS, FEDERAL REGULATORS AND OTHER SENIOR OFFICIALS FROM USDA, EPA, AND FDA HAVE MET AND EXCHANGED VIEWS WITH THE PRIVATE SECTOR, INCLUDING ENVIRONMENTAL GROUPS, REPRESENTATIVES FROM LARGE AND SMALL BIOTECHNOLOGY FIRMS, UNIVERSITY RESEARCHERS, STATE AND LOCAL OFFICIALS, MEDIA REPRESENTATIVES, AND PRIVATE CITIZENS WHO WERE INTERESTED IN THE ISSUES.

THESE MEETINGS HAVE SERVED AS A SPRINGBOARD FOR EXPLAINING THE DEPARTMENT'S POLICIES, PROGRAMS, AND REGULATIONS CONCERNING AGRICULTURAL BIOTECHNOLOGY. IN RETURN, THE PRIVATE SECTOR HAS HELPED THE DEPARTMENT IDENTIFY INFORMATION GAPS THAT NEED TO BE ADDRESSED. FINALLY, THE MEETINGS HAVE OPENED DOORS OF COMMUNICATION BETWEEN THE PUBLIC AND PRIVATE SECTORS.

CONCLUSION

WE ARE CONFIDENT THAT WE ARE MEETING OUR RESPONSIBILITIES IN A WAY THAT WILL MAKE THE PRODUCTS OF BIOTECHNOLOGY AVAILABLE TO OUR AGRICULTURAL COMMUNITY AS QUICKLY AS POSSIBLE WHILE ENSURING THAT FULL PROTECTION IS PROVIDED TO AGRICULTURE AND THE ENVIRONMENT.

ATTACHMENT
USDA Response to Request for Information
Sub-Committee on Natural Resources, Agriculture Research, and Environment
U.S. House of Representatives, May 5, 1988

1. Since October 1, 1986, the number of applications received by the U.S. Department of Agriculture (USDA) for review of planned introductions of genetically engineered organisms into the environment.

Answer: Between October 1, 1986, and July 16, 1987, USDA received 10 voluntary submissions requesting an opinion by USDA on the risk of plant pest introduction of a small scale, controlled field test. On July 16, 1987, the final rule (7 CFR 340) under the authority of the Federal Plant Pest Act and the Plant Quarantine Act applicable to genetically engineered organisms became effective. Between July 16, 1987, and the present, USDA received 23 applications for permits for release into the environment under the provisions of 7 CFR 340.

Between October 1, 1986, and the present, USDA received applications for U.S. veterinary biological product licenses under the authority of the Virus-Serum-Toxin Act of 1913 (VSTA) (9 CFR 102) for products derived by new biotechnological procedures as follows: Category one, 22 applications; Category two, three applications; Category three, no applications.

2. A general description of the types of organisms for which applications have been received since October 1, 1986.

Answer: (This answer is based on the assumption that the question applies only to applications for release.) The majority of the voluntary submissions and permit applications regulated under 7 CFR 340 by USDA were for herbicide tolerance in tobacco and tomato. Other tests were for insect, virus, and disease resistance in tobacco and tomato, and for genetically altered bacteria.

The U.S. veterinary biological product license applications received between October 1, 1986, and the present, were as follows: Category one products included monoclonal antibodies used as components in diagnostic kits for avian leukosis, canine parvovirus, feline leukemia, and feline infectious peritonitis; the Category two products were recombinant-derived modified live virus pseudorabies vaccines for use in swine.

3. The number of applications received since October 1, 1986, which have been approved.

Answer: (This answer is also based on the assumption that the question applies only to release into the environment.) Between October 1, 1986, and July 16, 1987, USDA responded to 8 voluntary submissions with opinion letters stating that the proposed field tests would not pose a risk of plant pest introduction. Between July 16, 1987 (the effective date of 7 CFR 340) and the present, 11 permits were issued by USDA for release into the environment of genetically engineered organisms subject to the provisions of 7 CFR 340.

Between October 1, 1986, and the present, USDA granted U.S. veterinary biological product licenses as follows: In Category one, 17 licenses; in Category two, two licenses for recombinant-derived modified live virus

pseudorabies vaccines for use in swine.

4. The number of applications received since October 1, 1986, which were denied.

Answer: No applications have been denied for permits under the provisions of 7 CFR 340 or for licenses under the provisions of 9 CFR 102.

5. The number of applications received since October 1, 1986, which required a request for further information by USDA.

Answer: USDA regulates on a case-by-case basis under the provisions of 7 CFR 340, and an environmental assessment is required before each permit for release can be issued. Because of the thoroughness of the environmental assessment, the principal reviewers for the permit applications estimate that about one-third of the applications for release involve a request for additional information from the applicant.

The requirements for a U.S. veterinary biological product license under the provisions of the VSTA are clearly defined to assure purity, safety, potency, and efficacy as provided in 9 CFR 113. If, for example, a proposed field test for a recombinant-derived modified live virus vaccine was not designed to produce the necessary safety data, the applicant would be notified before the tests were initiated.

6. The number of applications received since October 1, 1986, which were reviewed by USDA and at least one other Federal agency.

Answer: Between October 1, 1986, and July 16, 1987, the voluntary submission from Biotechnica, Inc., to USDA was also submitted to EPA for review. Between July 16, 1987, and the present, seven permit applications for release submitted to USDA under the provisions of 7 CFR 340 were sent to EPA for review because they involved macroorganisms genetically engineered to produce new substances intended for pesticidal purposes. Two permit applications were submitted to USDA for release of organisms deemed not to be a plant pest, and these field test proposals were reviewed by EPA. One permit application for release is being reviewed concurrently, with careful coordination, by USDA and EPA.

After an environmental assessment (EA) has been prepared for a veterinary biological product license for a recombinant-derived modified live virus vaccine, the EA is reviewed by the USDA Veterinary Services Biotechnology Committee, which includes a representative from the National Institutes of Health and a representative from the Food and Drug Administration.

Mr. SCHEUER. Thank you very much, Dr. Gilles.

I'm going to yield now to my minority colleague, Congrsswoman Claudine Schneider.

Miss SCHNEIDER. Thank you.

Dr. Wyngaarden, some time ago, the Committee on Science and Technology did its report on biotechnology, and at that time there was some concern that some of the definitions included in the BSCC were not clear enough. Dr. Kingsbury was there at the time, and he said by 1987 all of those definitions should be completed and then published.

Are we now in a situation where the definitions are completed and published?

Dr. WYNGAARDEN. That has proved to be a much more complex issue. I think any layperson would think that definitions, imagine that once you get together, you could very quickly agree on such.

It turns out that it's almost impossible to get people across disciplines to agree on any one definition. It deals with pathogens, environmental release, containment, or any other—what is a recombinant organism, what is a genetically modified organism.

In practice, what has happened is that there is an operational definition within each regulatory agency. We just came back, as I mentioned, from the OECD meeting in Paris, and one of the first items on that agenda was definitions. We appointed a working group on definitions which met for two days and came away feeling that there was no possibility of agreeing.

Miss SCHNEIDER. No possibility of—

Dr. WYNGAARDEN. No possibility of agreeing.

Miss SCHNEIDER. Terrific!

Dr. WYNGAARDEN. Among the countries. We appointed a working group to continue to deliberate that issue over the next year. When it came to giving priorities among six or seven such topics, that one came out at the absolute bottom, because the general feeling was that it wasn't feasible.

Mr. SCHEUER. Would my colleague yield?

Miss SCHNEIDER. Yes, I'd be glad to yield.

Mr. SCHEUER. Dr. Wyngaarden, if nobody can agree on anything, where does that leave industry?

Dr. WYNGAARDEN. Well, it leaves industry dealing with each agency, and there are working definitions, and I don't think they're that disparate. It's just when you come to the limits of a definition, you essentially have to set some sort of an operational strategy.

For example, the issue of containment. The EPA has its definition of containment, and when something is done that's outside those limits of containment, it automatically becomes an environmental release.

Now their definition is not precisely the same as that of the Agriculture Department or of the FDA.

But you raise a very good point, and one of the issues that we—

Mr. SCHEUER. I mean, don't you think that industry is entitled to something a little more helpful and a little more specific than that?

Dr. WYNGAARDEN. We are planning our first open meeting since I became chairman. It's scheduled for June. One of the issues we are going to discuss with industry is, what are the problems that

they are having dealing with the federal Coordinated Framework and with the individual agencies. If they have serious problems with the definitions, we will raise those to a level of priority to address them. We have not really seen that.

Mr. SCHEUER. Well, look, I'm not an expert on this subject, and I'm going to yield back to Congresswoman Claudine Schneider.

But I think it's very important for the involved federal agencies to get their acts together and to give industry some clear guidelines on what the parameters are, what their roadmap is. I think it's absurd that the Government can't do that.

Dr. WYNGAARDEN. Well, I think we have done that, Congressman. I think there's some ambiguity as to what is a pathogen, for example, but that is not impeding progress in this field. There is a general rule of reason understanding of what deliberate release is, and I think that is allowing people to go forward very well.

Mr. SCHEUER. Well, we will have some further discussion of this, perhaps in a subsequent hearing on exactly this point. But it seems to me, when you force industry to move ahead and tiptoe through the mine field under a set of rules where each agency has its own definitions, you're crippling them.

You know, they are functioning in a competitive, a bitterly competitive international economic environment in the global marketplace, and we want to unleash industry to do the best they can, to be the most effective competitors they can, and we don't want to burden them. We don't want to hold them back. We don't want to burden them with either unnecessary financial constraints or time constraints in trying to figure out which is the path through the mine field, and I think it's incumbent on the agencies to get together and give industry a clear bunch of definitions, so that they have a clear roadmap as to where they can go and what the parameters are within which they must function.

Dr. WYNGAARDEN. Well, we're trying to do that, and I would like to stress the shift in emphasis that has occurred in the science base over the last few years.

Rather, for example, than regulating recombinant DNA organisms or genetically-modified organisms or some other definition of organism type based on the method of production of that organism, we want to shift toward generic guidelines in the development of organisms for release and the classification of those based on the risk involved. There are very low-risk organisms, ones that contain slightly more risk, on up to ones that might be somewhat dangerous, and the rules would differ for that.

In addition, we have this proposal from the National Academy of Sciences to take a hard look, sort of an extension of the Kelman study on environmental release, to take a hard look on the science base underlying this industry, and definitions will be one of the things that they will be asked to look at.

Mr. SCHEUER. I yield again to my colleague, Congresswoman Schneider.

Miss SCHNEIDER. The BSCC is responsible for evaluating the environmental impact.

Dr. Moore, I'd like to address this question to you. But I'm interested in knowing to what degree are we monitoring or regulating some of the long-term social effects?

For example, CIBA-GIEGY is working on increasing the resistance of certain crops to herbicides, so that they might be able to use more herbicides on some of the weeds. Now in my humble opinion, the likelihood of an increase in groundwater contamination, I would think, would be rather extreme.

To what degree do you have regulations in hand or guidelines in hand to ask those kinds of questions about secondary social impacts?

Dr. MOORE. Congresswoman, staying with your theoretical example, if a company wanted to develop pesticide resistance in a plant, and that pesticide was known to be a potential problem or a real problem in groundwater, that certainly would be a negative factor that we would want to examine in great detail prior to allowing that to go to commercial production, because as you postulate, you could exacerbate the very conditions of leaching, and indeed it could, in certain circumstances or certain areas, it may well be that one would not license or would not allow the use of that material in areas that were very vulnerable to groundwater contamiantion.

Miss SCHNEIDER. So you do have a set of guidelines that look at those secondary impacts?

Dr. MOORE. Yes.

Miss SCHNEIDER. And do each of your other respective agencies also have that kind of criteria for review.

Dr. GILLES. Yes.

Miss SCHNEIDER. Secondary impacts?

Dr. WYNGAARDEN. The Recombinant DNA Advisory Committee would look at those to assess things that came before it.

Miss SCHNEIDER. I'm interested in knowing about whether or not you think that there are adequate opportunities to inform the public in terms of public hearings and discussions in an open forum.

Prior to the June 1986 publication of the Coordinated Framework, there was a lot of criticism from various citizens groups, saying that the BSCC didn't provide enough openness, enough discussion of the BSCC process.

What would be your assessment today?

Dr. WYNGAARDEN. Well, we've had several public meetings. We had one on the BSCC in the National Academy of Sciences auditorium that was announced, and many people came, not as many as we thought might come, but many did. And we've had subsequent open meetings.

We're planning another one in late June, early July. The date is not quite fixed yet. And one of the major purposes of that open hearing is to hear from the biotech industry and university scientists, how they think the BSCC mechanism is functioning.

This is an evolving matter, and we've already made some changes in it, as I think Chairman Scheuer cited in his opening remarks in the case of USDA and EPA, and I have no doubt that it will evolve in somewhat the way that the Recombinant DNA Advisory Committee of the NIH did. That has been revised now numerous times as we've had more experience. I think the same thing will happen here.

Miss SCHNEIDER. And have your agencies, are you also under the opinion that there has been adequate opportunity for public participation?

Dr. MOORE. I think there's been adequate opportunity for public participation on the BSCC proposals, and I also feel that in addition to that, there has been a routine opportunity for public comment on any proposed field experiment, which is really where the intense interest often is generated.

I might also make one other comment as it relates to coordination of activities. Our review process has been open, and people can listen to it, can comment on it.

The other thing is, the process that we have used, as far as trying to coordinate across agencies, for example there are some places where there is overlapping jurisdiction. In almost every instance, since the framework has been announced, where there's been commonly overlapping jurisdiction between USDA and EPA, we have agreed that we would work from a common review and a common database and then applying what would be appropriate to our statutes.

Dr. GILLES. Congresswoman, I also indicate affirmatively that I think we have ordered an opportunity for open debate. When we went to the final rule on plant pest regulations, we had three open hearings—in the West in San Francisco, in the Midwest, and here in Washington, D.C., and as I indicated in my opening remarks, we've had five hearings—not hearings, but actual two-day sessions with respect to challenge of public perception, and these have been quite well attended.

I think your term was modified by the term "adequacy," and I guess one would require some definition. The opportunity has been there, and we also do publish in the Federal Register to permit people to comment on any changes in the rules that we have made, and we certainly have had and encouraged participation by the written word as well.

Miss SCHNEIDER. Okay. The last question that I had, long-term research goals, what do you gentlemen perceive as being a few of the long-term research goals that we ought to be looking into?

Dr. Moore, you had mentioned that you had received nine applications, I believe you said under FIFRA, and that nine had been approved. And I wonder, as you are reviewing these, are you coming to some kind of general consensus that there ought to be certain long-term research goals that we're focusing on.

Dr. MOORE. I think that something that we can't lose sight of is the database from which we all collectively must make that judgment as to what degree of risk may be associated with a proposed use. I still think that there are areas of research that need to be addressed to allow us to better hone in our ability to do that and do that with a fair degree of precision.

Something that we have done with some of these early field tests is, the tests are limited in scope, and we require that the results of those tests be made available to the agency, so that we can use that as a gauge as to whether or not our interpretation of the experiment, absent the data, is correct, and based on the real data, we then can modify, if you will, some of our judgments.

But some of these interactive things from an ecological standpoint are still not well underpinned, as well underpinned as we would like them to be, as far as making informed judgments prospectively.

Miss SCHNEIDER. Okay. Thank you. I do regret that I have to run over and vote now. So take it away, Tom.

Mr. MCMILLEN [PRESIDING]. Thank you very much. Well, I have voted. I'm sorry that I have missed some of the early parts of the hearing, but we've had rapid-fire votes today, so I've been over on the floor.

I did have some questions for each of you that I would like to pose and get some responses on.

To Dr. Moore first, you and others from the EPA have publicly discussed your thoughts about creating Environmental Biosafety Committees or EBCs to review field test proposals at universities.

The first question I have is, can you explain to us how the EBC system would work?

Dr. MOORE. Well, as we sit here today, it still is a concept as opposed to a reality. But what we see is—first of all, we see a need to look more than a few weeks or a few months ahead. We envision a time within a matter of a few years whereby the number of proposals that will be submitted will be of such a magnitude that to continue to entertain them only at Headquarters at EPA would stifle the whole process, because we just don't have the manpower to be able to turn them around in a real-time fashion.

So what we were looking for was an ability to speed up the process, but not do anything to impugn the integrity of the product that comes out of the process. The best way that we know of doing that is to try to enlist the expertise that is typically found in academia through this EBC mechanism that could be set up by academia or in regionalized areas across the country and working under a general set of criteria that would describe the expertise that needs to be on the committee and the types of factors that need to be considered in reviewing any of these applications, we hopefully could get expert judgment as to whether or not they should go forward, and if so, under what conditions and still get them in a real timeframe that's needed if we aren't going to stifle this industry.

Mr. MCMILLEN. The same question I had is, under what authority is EPA delegating its responsibility for enforcing TSCA to private local review groups?

Dr. MOORE. Well, the way we would propose to do that is by basically saying that we have—well, the framework that we identified a couple of years ago revoked an R&D exemption that existed under TSCA in saying that it's related to microbials of one sort or another, there is no exemption. Now what we're saying is that you must come to EPA and provide certain types of information unless you have submitted your application to an EPA-approved Environmental Biosafety Committe, and they in turn have approved the experiment.

That would only apply to an early R&D phase under what would probably be a very well-defined list of organisms, and what I have just described would be done under the authority of the Toxic Substances Control Act. That certainly has to be done through pro-

posed rulemaking, which we hope to come out in the next couple of months and then go to final rule.

Mr. McMILLEN. Dr. Moore, in the Coordinated Framework, EPA indicated that it would soon be publishing rules to implement its proposed regulation of biotechnology products under the Toxic Substances Control Act.

Given the importance of this Act in the regulatory scheme as the regulatory safety net, the Committee on Science and Technology recommended that the agencies give the highest priority to complete the rules needed to make the Coordinated Framework enforceable.

Has EPA published the final rules?

Dr. MOORE. No, Congressman, we have not promulgated those rules yet. Those are the rules I was referring to just a minute ago that we hope to have coming out this summer.

One of the main problems, main obstacles, that we faced was also alluded to by Dr. Wyngaarden a few minutes ago. We had proposed that the definition of "pathogen" would be somewhat of a switching mechanism which would capture certain things under those rules or not capture them, and based on a variety of comments that we received and reanalysis, as well as referring it to our outside expert committee, we had to come to the conclusion that trying to use the word "pathogen" as that switching mechanism for rulemaking just was not going to be scientifically sound.

When we lost that mechanism, we had to come up with an alternative mechanism, which has accounted to some large degree for the delay in the original timetable that we had set out for ourselves.

Mr. McMILLEN. If you can't come up with a definition of "pathogen," what will determine which genetically-engineered organisms will be reviewed under the Act?

Dr. MOORE. Well, what we are looking at are a series of mechanisms. One of the mechanisms that was identified a couple of years ago were intergeneric combinations. Any transfers involving organisms from two different taxonomic genera would be captured for review. And what we're also talking about is capturing other things that would represent other types of altered organisms or normal organisms that were proposed to be used in an unnatural environment, and we would have to do that through rulemaking and a listing of organisms. That's our thought process that we're looking at right now.

Mr. McMILLEN. Switching gears, I'd like to ask Dr. Wyngaarden a few questions.

I know that you've already been asked a number of questions, but one of the points of emphasis is reducing the duplication that currently exists.

Could you summarize your feelings on how we resolve the overlapping jurisdictions of the EPA and the USDA with respect to field study reviews?

Dr. WYNGAARDEN. Well, it has turned out to be less of a problem than we had anticipated. We have, first of all, arranged since last year to exempt certain applications from compulsory review by the NIH RAC, if they also fall under one of the other agencies, and

there have been particular examples where that has been resolved rather quickly and easily.

There have also been some areas in which there have been consultation between and even joint review by the EPA and the USDA where I think that has proved to be workable within the general framework of the BSCC and the coordinated guidelines.

Mr. MCMILLEN. Will the BSCC commit to a timetable by which an appropriate resolution of this jurisdiction problem can be expected by Congress?

Dr. WYNGAARDEN. Well, the BSCC is coordinating and advisory, and the regulations govern what the regulatory agencies can and must do. We don't have any authority to interfere with that. If some of these are brought for discussion and resolution at the committee meetings, we seem to manage to work out those matters rather easily just by sitting down together. But the statutes gather what EPA and what USDA must regulate.

Mr. MCMILLEN. Dr. Gilles, has the USDA resolved the division of responsibility over biotech agricultural product reviews?

Dr. GILLES. The agricultural product reviews?

Mr. MCMILLEN. Yes, as mandated by the Coordinated Framework.

Dr. GILLES. I think that that has been quite well resolved. The products that need to be considered are reviewed primarily at this point in time by APHIS, and we have a Biological Coordinating Committee (CBA) within the USDA that handles these matters, so that various agencies that may need to have input or may serve as resources in the system as evaluating the issues are informed. And I believe the system is working quite well.

Mr. MCMILLEN. Are there two separate areas of USDA that have jurisdiction or purview over biotechnology?

Dr. GILLES. Yes. One is the research area; the other is the regulatory area. And in general, there are three areas in research: the Forest Service, the Agricultural Research Service, and the Cooperative State Research Service, and to a lesser degree, the Economic Research Service.

Within the area of the regulatory, there are three agencies: the Animal and Plant Health Inspection Service, the Food Safety Inspection Service, and the Agricultural Marketing Service.

Mr. MCMILLEN. Maybe one last question is, what can we do to minimize the efficients—maximize, excuse me—the efficiency of USDA's review process for biotech agricultural products?

Dr. GILLES. Well, I think we're endeavoring to do that internally, and I'm not aware that this is a problem. We have stated that there is a certain procedure, and we have inserted timeframes when the procedure must be completed, and to my knowledge, each of the applications that we have received to date have met that timeframe.

Mr. MCMILLEN. I guess one concluding question that I might ask is, is the pace of applications for field testing increasing in your view? Anybody who wants to answer that.

Dr. GILLES. I think the pace is; however, field testing must be put in the perspective that it is somewhat seasonal. People usually, of course, are concerned about doing it sufficiently early, so that they

can get in the appropriate growing season. So to that degree, the amount of work varies from season to season.

And in terms of the number of applications, yes, the number of applications are increasing.

Mr. McMILLEN. Are the agencies reviewing them more quickly, these applications?

Dr. GILLES. As I mentioned earlier, I think that we have a system in place, that there has been no problem, so far as I'm aware, and in certain instances, as Dr. Moore indicated, we have shared information and shared data with EPA where there was any concern that there might be any interest or, say, a TSCA or a FIFRA regulation that might be applicable, in contrast to those within the Plant Pest Act, for example, and I think the sharing of information has also gone along quite well.

Mr. McMILLEN. Dr. Moore, do you have any comments on that?

Dr. MOORE. Well, from EPA's perspective, the number of applications has gone up numerically over time in the last couple of years. I must say, however, that I think our feeling is that the increase in applications, as it relates to microbial products for experimental release has probably not gone up as fast as we might have anticipated a couple of years ago, and I have no explanation for that.

Mr. McMILLEN. With the, I guess, increase in applications, have you also found that companies are getting better at providing the right—submitting the right data with the application?

Dr. MOORE. Yes. As is true of anything, I think people watch very closely for the types of information you're asking on a series of organisms, and after we had done two or three and given the public nature of the process, they quickly, I think, get to understand what it is that's going to be required to be in their package, and so therefore it arrives with the first shipment, if you will, rather than have to go back with a recycle because the agency says, gee, you're missing this or you're missing that.

I think it also has helped that when they've got the sense that the nature of information that EPA and USDA want is quite similar, that also speeds up the process.

Dr. GILLES. If I might add, I think one of the concerns, of course, has been the concern of uncertainty, and after you have tried a process and learned what the procedures are, the uncertainty is minimized. And I hope and I do believe that the efficiency is increasing.

Mr. McMILLEN. What—in your view, how long will it be before the agency receives a request for full-scale test or commercial use?

Dr. GILLES. For commercial use?

Mr. McMILLEN. Yes.

Dr. GILLES. I'm afraid I'll have to ask for a clarification. What do you mean by a full-scale test?

Mr. McMILLEN. Right now, we're talking about small- scale and just moving into the full-scale tests.

Dr. GILLES. Well, I think I would have to respond, it certainly depends upon the success of the small-scale tests.

Dr. MOORE. I don't see any likelihood of a request for a full commercialization, a full field testing as the last stage of going to commercialization, dealing with microbes in the environment in the next couple of years. I don't see it at all.

We have had one commercial request, which I believe we have granted, which involved creation of a pesticide using an engineered organism, but that organisms was killed before it would be used in the environment, and I don't think that's relevant to the nature of the question of you're asking.

Mr. MCMILLEN. Well, in my own district, Crop Genetics International is a—the feasibility, I guess they'd have to go into the next season to get some data, but I mean, how long will that process take?

Dr. MOORE. Maybe an example might be, one of the first tests that was approved was the ice-minus bacteria out in California, performed by AGS. Based on the results of that experiment, they have come back and have proposed additional experiments, an increase in breadth. I would still call them small-scale, although there's probably a series of experiments being evolved right now.

Mr. MCMILLEN. I'm just curious. How many years, I mean, I'm just—how many years of small-scale tests—

Dr. MOORE. Several years, I think.

Mr. MCMILLEN. Several years. Is that two, three?

Dr. MOORE. Two, three, five. I don't see it—

Mr. MCMILLEN. And then if you came back with proper information, you could move forward with a full-scale test?

Dr. MOORE. Yes.

Dr. GILLES. Congressman, if I might respond from the standpoint of the agricultural experiment stations, generally when you try to work with plants, you usually rely on three years or three seasons of testing, primarily to make sure that you have—two factors; one is genetic stability, and two, the environmental factors, so that you don't want to easily move forward and find what went as a very good test in a succeeding year, when the environmental conditions were different, would become an improper test or a failure. I would say three to five years minimum.

Mr. MCMILLEN. On the small-scale tests, right?

Dr. GILLES. Yes, sir, before you go to a large- scale test.

Mr. MCMILLEN. Again we're dealing in kind of outward years in the future. But what I'd be curious about, in response to what you just said there, how do the agencies monitor field tests to measure possible adverse environmental effects? And this could obviously change, as you said, from year to year really, based on your comments.

Dr. GILLES. Well, if you're dealing with plants, for example, you'd need to be concerned about the water and the temperature and these types of things. And certainly tests are going on now to test the yields, to test the movement of the bioengineered products, and surveillance of these types of activities is assured.

Mr. MCMILLEN. The other—I guess the final question that I have is, what is the utility of the OTA report as it pertains to large-scale field testing? What does all this mean?

Dr. MOORE. Congressman, I haven't had a chance to read and reflect upon the contents of the OTA report, but based on the summary of it that I have read, I think it correctly identifies the fact that some of the early field tests, based on even results that we are receiving from those tests, suggest that these pose negligible risks or the nature of those tests have posed negligible risks to date, but

that one doesn't want to necessarily become overconfident as you get into large-scale or into commercialization.

And I think it's quite clear, however, that the results of some of these small-scale tests will refine our ability to predict with confidence the likelihood of the results of some of these large-scale tests, but there's no question as well that in going to large-scale tests, the nature of some of the questions that would be asked may also change as you increase in size.

Mr. McMillen. Maybe elaborate on that point just a little bit, give me some of your thoughts on that.

Dr. Moore. Well, small-scale tests are usually well-defined as to where the geographic area is, what is the plant life that's going to be in the test area, what is the plant life that's in the area immediate adjacent to the test plot. There usually is a buffer zone. And then what is the plant life that is around that? What is the biota that may fly in or blow through is a part of that test.

That's fairly easily defined, comparatively speaking, when you're talking about a small experiment. When you then take that same experiment and propose to do it, say, rather than just in one location in Maryland, but you want to do it in 20 locations widely disparate across this whole country, the type of biota that may be in the surrounding areas is likely going to change, assuming that you don't pick identical sites as the same in your first site.

The other way I could give you as an example were the first two ice-minus experiments that the agency reviewed. One involved the application of material on a blooming shrubbery plant. The other one proposed that the ice-minus material would have been applied to a potato at the time it was planted, and then it was also going to involve application once the potato plant had sprouted.

Obviously in one instance, one wanted to focus on the possibility that you would attract honeybees and what would likely be the outcome of the honeybee coming in contact with the material, as well as having to ask the legitimate question, where is that bee going to go after it's left that plant. That probably is a much more germane question in that experiment than it would be when you talked about the potato plant where it was going to be innoculated on the seed which was then deposited in the ground. A different set of questions would be involved in that circumstance.

Mr. McMillen. Well, let me, just for the sake of my edification, let me go back to the corn borer for a moment and Crop Genetics, and what I'm interested in is where there will be two tests, two small one-acre tests, being conducted. Obviously this blight causes $400 million in economic losses a year, and you'll do these one-acre tests, and three to five years, just extrapolating outward, if everything goes along the path smoothly, then you would move to a full-scale test, presumably several locations, and again what time—a three to five-year timeframe again, is that—I'm just in my own mind trying to—I'm not trying to pin you down. I'm trying to get your sort of estimation on some timeframes here.

Dr. Gilles. As much as I was the one who responded to the timeframe, it's obviously an estimate. But basic work on plant research, those types of timeframes have been used in the past, and I think certainly the experience that is gained in the small-scale tests within that first, probably three-year, timeframe would certainly

set the scene as to how quickly you could expand to a much larger area.

In all probability, though, if all factors went according to plan, and hopefully they would, I would think that they would be able to move, then, rather quickly into large-scale tests. Once they concluded with assurance that the small-scale tests were able to be repeated, were able to be replicated, and served both the assurance that there would be no danger to the environment and the opportunity for economic enhancement, I'm sure these types of factors will be uppermost in the minds of those people that are developing the system.

Mr. McMILLEN. How does that compare to traditional breeding timetables?

Dr. GILLES. Well, obviously it depends on what type of plant you're dealing with. Traditional breeding for wheat, for example, will take approximately 15 years. You might cut it down, as we did in the spring wheat area, by crossing and planting in the spring and then taking to Mexico or Southern California for winter increase, and then returning to the spring wheat area.

Using, of course, hybrids in corn, that time has substantially been reduced.

Mr. McMILLEN. Basically we're talking about comparable periods of time to take this to a commercial level.

Dr. GILLES. I think at the onset perhaps. Then once we achieve a point where we understand the system and we are assured that there is safety, then I think the timeframe doubtless will be reduced.

Mr. McMILLEN. Well, I certainly appreciate your comments. I didn't get a chance to say this in my introductory comments, but biotechnology is a very, very important industry to the State of Maryland. I think we are No. 3 in the country in terms of resident biotechnology firms, and we, as well, have a lot of the regulatory structure as well in our state, so we have a keen interest not only in the regulatory side, but in the advance of the industry.

I appreciate your coming by, and I'm sure if the chairman was here, he would like to echo those comments and close on that note.

Thank you.

[Whereupon, at 4:35 p.m., the subcommittee was recessed, to reconvene at the Call of the Chair.]

88-743 (105)